66321

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SEARCH REQUEST FORM

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Scientific and Technical Information Center

Equivalent claims in U.S. Parent 10/047,434 (ISTIC)

Requester's Full Name: MOLLY CEPERLEY Examiner #: 59757 Date: 05/09/02

Art Unit: 1641 Phone Number 308-4239 Serial Number: PCT/US01/50838

Mail Box and Bldg/Room Location: CM1-8D15 Results Format Preferred (circle): PAPER DISK E-MAIL

↳CM1-8E12

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: MASS TAG FOR QUANTITATIVE ANALYSIS

Inventors (please provide full names): Haihong Zou

Earliest Priority Filing Date: 10/25/00

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

① Please search for each of the compounds of claims 19-22.

② Please search for the concept of PROTEIN IDENTIFICATION, PROTEOME ANALYSIS, PROTEIN ANALYSIS using "PROTEIN MASS TAG (PMT)", ISOTOPE-CODED AFFINITY TAG (ICAT), DIFFERENTIAL LABELING FOR MASS SPECTROMETRY

or

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher: Shelley Gambel	NA Sequence (#)		STN	
Searcher Phone #: 308-4499	AA Sequence (#)		Dialog	
Searcher Location:	Structure (#)		Questel/Orbit	
Date Searcher Picked Up:	Bibliographic		Dr.Link	
Date Completed: 5/11/02	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:	Fulltext		Sequence Systems	
Clerical Prep Time:	Patent Family		WWW/Internet	
Online Time:	Other		Other (specify)	

PTO-1590 (8-01)

Considered
05/25/02
MEC

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 19:36:17 ON 10 MAY 2002
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FILE COVERS 1907 - 10 May 2002  VOL 136 ISS 19
FILE LAST UPDATED: 8 May 2002  (20020508/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

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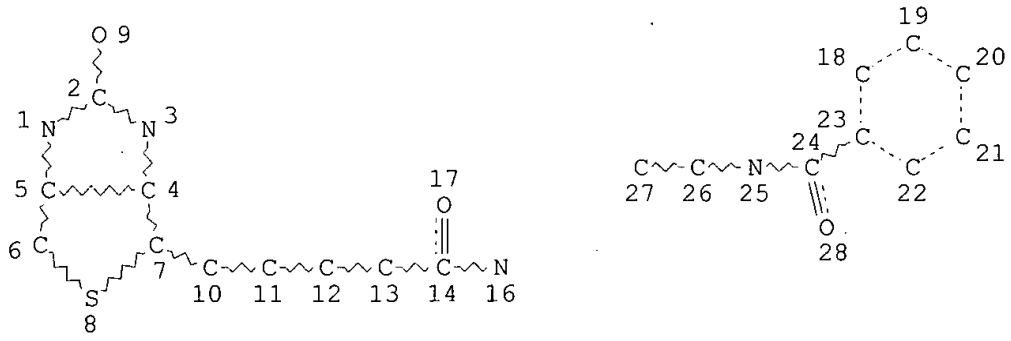


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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS  27

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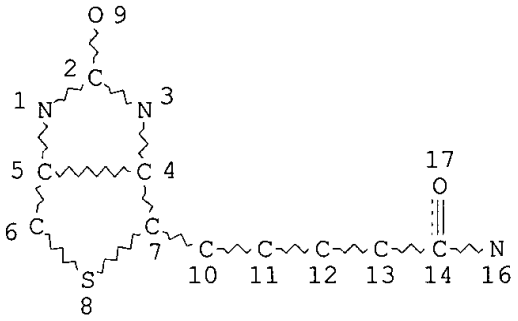

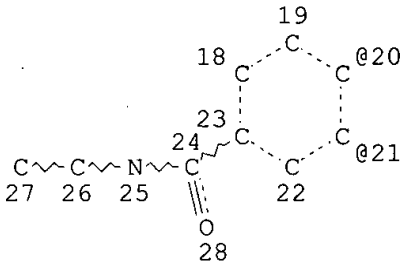

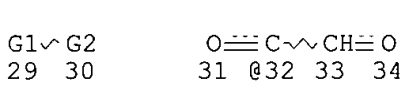

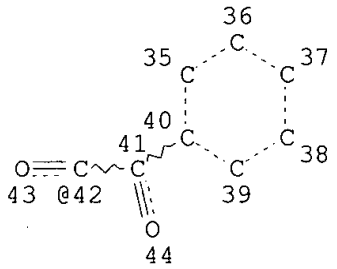

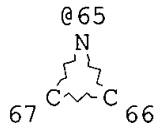

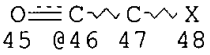

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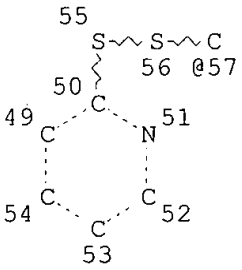

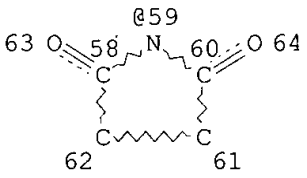

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 66

STEREO ATTRIBUTES: NONE
L7 1 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L8 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L7

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=> d ibib abs hitrn l8 1

L8   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:923565  HCAPLUS
DOCUMENT NUMBER:          136:42919
TITLE:                    Biotin derivatives for an extracorporeal device
INVENTOR(S):              Sandberg, Bengt; Wilbur, Scott; Nilsson, Rune
PATENT ASSIGNEE(S):       Mitra Medical Technology AB, Swed.; University of
                          Washington
SOURCE:                   PCT Int. Appl., 45 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.   DATE
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     WO 2001095857      A2   20011220       WO 2001-SE1374    20010618
     WO 2001095857      A3   20020328
         W:  AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES,
             FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
             MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ,
             TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                  SE 2000-2287      A  20000616
                                        US 2000-216625P   P  20000707

AB   A method for the conditioning of an extracorporeal device is described, as
     well as a method for extracorporeal extn. of toxic material from mammalian
     body fluids in connection with diagnosis or treatment of a mammalian
     condition or disease.  The methods comprise (i) a soln. contg. a reagent
     comprising biotin moieties, such as natural biotin or its derivs., and a
     toxin-binding moiety, (ii) linkers and a trifunctional crosslinking
     moiety, and (ii) an extracorporeal device comprising said reagent.  For
     example, a dibiotin compd., 1-isothiocyanato-3,5-bis-(13'-biotinamidyl-
     4',7',10'-trioxatridecanamidyl)-aminoisophthalate was prepd. and
     conjugated with a toxin-binding mol., i.e., monoclonal antibody 53-6A2.  A
     dibiotin-toxin-binding conjugate was used for conditioning of an
     avidin-agarose column suitable for removal of toxins from blood.
IT   380607-53-4P
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (prepn. of biotin derivs. for conditioning of extracorporeal device and
        extn. of toxic material from mammalian body fluids)


=> fil caold
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FILE COVERS 1907-1966
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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L9 0 L7

=> fil reg
FILE 'REGISTRY' ENTERED AT 19:36:47 ON 10 MAY 2002
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STRUCTURE FILE UPDATES: 8 MAY 2002 HIGHEST RN 412906-88-8
DICTIONARY FILE UPDATES: 8 MAY 2002 HIGHEST RN 412906-88-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can l7

L7 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 380607-53-4 REGISTRY
CN 1,3-Benzenedicarboxamide, 5-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)-N,N'-bis[19-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-15-oxo-4,7,10-trioxa-14-azanonadec-1-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C52 H79 N9 O14 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

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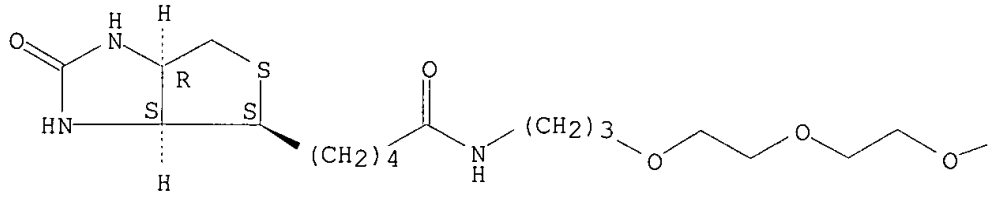

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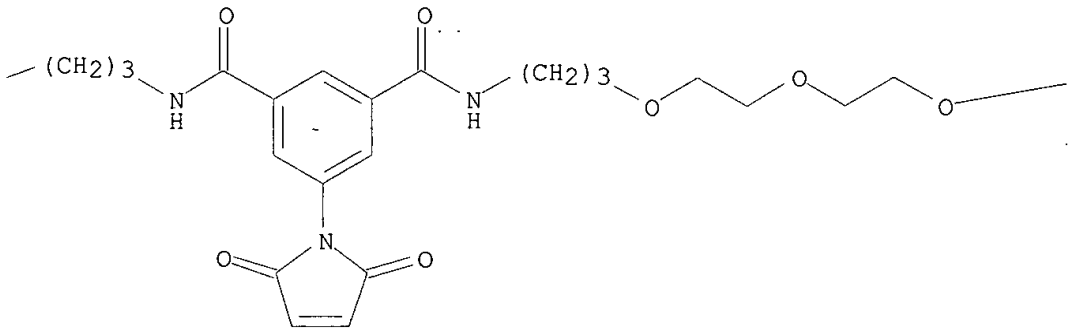

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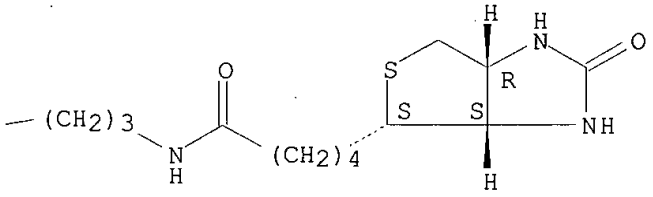

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:42919

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FILE COVERS 1907 - 10 May 2002  VOL 136 ISS 19
FILE LAST UPDATED: 8 May 2002  (20020508/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

CAS roles have been modified effective December 16, 2001. Please
check your SDI profiles to see if they need to be revised. For
information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

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L6              STR
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L8            1 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L7
L10             STR
L11          89 SEA FILE=REGISTRY SUB=L5 SSS FUL L10
L12          33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11
L13          32 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L12 NOT L8


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=> d ibib abs hitrn l13 1-32

L13  ANSWER 1 OF 32  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:293894  HCAPLUS
TITLE:                    High throughput or capillary-based screening of
                          libraries of compounds for biological activities
INVENTOR(S):              Short, Jay M.; Keller, Martin; Lafferty, William
                          Michael
PATENT ASSIGNEE(S):       Diversa Corporation, USA
SOURCE:                   PCT Int. Appl., 229 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   7
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PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002031203	A2	20020418	WO 2001-US31806	20011010
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
US 2001041333	A1	20011115	US 2000-738871	20001215
US 2002048809	A1	20020425	US 2001-790321	20010221
US 2002015997	A1	20020207	US 2001-894956	20010627

PRIORITY APPLN. INFO.:

US 2000-685432 A2 20001010
US 2000-738871 A2 20001215
US 2001-790321 A2 20010221
US 2001-894956 A2 20010627
US 2001-309101P P 20010731
US 1997-876276 A2 19970616
US 1998-98206 A2 19980616
US 1999-444112 A2 19991122
US 2000-636778 A2 20000811
US 2000-687219 A2 20001012

AB Provided is a method of screening or enriching a sample contg. polynucleotides from a mixed population of organisms. The method includes creating a DNA library from a plurality of nucleic acid sequences of a mixed population of organisms and sepg. clones contg. a polynucleotide sequence of interest on an analyzer detects a detectable mol. on a probe or bioactive substrate. Individual members of the library can be sepd. and analyzed using an ordered array of fine capillaries that can be used to take up individual members of the library. The capillary array may contain up to 1 million members. Methods of analyzing biol. activities, such as enzyme assays or reporter gene expression, are described. The analyzer includes FACS devices, SQUID devices and MSC devices. The sepd. or enrich library can then be further process by activity based screening or sequence based screening. In addn., the enriched sequence can be compared to a database and to identify sequences in the database which have homol. to a clone in the library thereby obtaining a nucleic acid profile of the mixed population of organisms.

IT INDEXING IN PROGRESS

IT **412319-47-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. and reactions of; high throughput or capillary-based screening of libraries of compds. for biol. activities)

IT **412319-48-3**
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(prepn. of, as assay substrate for esterases; high throughput or capillary-based screening of libraries of compds. for biol. activities)

L13 ANSWER 2 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:468181 HCAPLUS
DOCUMENT NUMBER: 135:73673
TITLE: Assay compositions and kits using chemiluminescent compounds and photosensitizers activating oxygen to

its singlet state
INVENTOR(S): Ullman, Edwin F.; Kirakossian, Hrair; Pease, John S.; Daniloff, Yuri; Wagner, Daniel B.
PATENT ASSIGNEE(S): Dade Behring Marburg G.m.b.H., Germany
SOURCE: U.S., 38 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6251581	B1	20010626	US 1991-704569	19910522
US 5340716	A	19940823	US 1991-718490	19910620
CA 2069145	AA	19921123	CA 1992-2069145	19920521
NO 9202009	A	19921123	NO 1992-2009	19920521
EP 515194	A2	19921125	EP 1992-304630	19920521
EP 515194	A3	19931020		
EP 515194	B1	20011031		
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AU 9217068	A1	19921126	AU 1992-17068	19920521
AU 657134	B2	19950302		
IL 101945	A1	19980208	IL 1992-101945	19920521
IL 116300	A1	19990411	IL 1992-116300	19920521
EP 984281	A2	20000308	EP 1999-121547	19920521
EP 984281	A3	20000607		
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EP 984282	A2	20000308	EP 1999-121551	19920521
EP 984282	A3	20000607		
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AT 208039	E	20011115	AT 1992-304630	19920521
JP 05180773	A2	19930723	JP 1992-131039	19920522
US 5578498	A	19961126	US 1993-156181	19931122
US 5536834	A	19960716	US 1995-471131	19950606
US 6180354	B1	20010130	US 1995-480430	19950606
US 5811311	A	19980922	US 1995-488228	19950607
US 5780646	A	19980714	US 1996-660029	19960606
US 6340599	B1	20020122	US 1998-75264	19980511

PRIORITY APPLN. INFO.:

US 1991-704569	A	19910522
US 1991-718490	A	19910620
EP 1992-304630	A3	19920521
IL 1992-101945	A3	19920521
US 1993-156181	A3	19931122
US 1995-471131	A1	19950606
US 1995-488228	A1	19950607

AB Compns. and kits are disclosed for detg. an analyte in a medium suspected of contg. the analyte. One method comprises treating a medium suspected of contg. an analyte under conditions such that the analyte, if present, causes a photosensitizer and a chemiluminescent compd. to come into close proximity. The photosensitizer generates singlet oxygen and activates the chemiluminescent compd. when it is in close proximity. The activated chemiluminescent compd. subsequently produces light. The amt. of light produced is related to the amt. of analyte in the medium. Preferably, at least one of the photosensitizer and chemiluminescent compd. is assocd. with a surface which is usually a suspendable particle, and a specific binding pair member is bound thereto. Prepn. of assay reagents and assays for vitamin B12, digoxin, human chorionic gonadotropin, TSH, and a target oligonucleotide are described. The digoxin assay used digoxin conjugated

with 6-carboxyfluorescein via a linker from bis-(3-aminopropyl)methylamine, biotinylated monoclonal antibody to digoxin, avidin conjugated with polystyrene beads contg. dioctadecylaminocarboxylbenzal acridan as acceptor beads, and anti-fluorescein monoclonal antibody conjugated with polystyrene beads contg. tetra-(n-decyl)aluminum phthalocyanin as sensitizing beads. After addn. of the sensitizing beads and incubation in the dark for 30 min at room temp., the reaction mixts. were illuminated for 1 min and chemiluminescence was detd. using a luminometer.

IT **346403-99-4**
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(assay compns. and kits using chemiluminescent compds. and photosensitizers activating oxygen to singlet state)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:408721 HCAPLUS
DOCUMENT NUMBER: 135:134197
TITLE: Biotin reagents for antibody pretargeting. 5. Additional studies of biotin conjugate design to provide biotinidase stability
AUTHOR(S): Wilbur, D. Scott; Hamlin, Donald K.; Chyan, Ming-Kuan; Kegley, Brian B.; Pathare, Pradip M.
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chemistry (2001), 12(4), 616-623
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An investigation was conducted in which the stabilities of four structurally different biotin derivs. were assessed with regard to biotinamide bond hydrolysis by the enzyme biotinidase. The biotin derivs. studied contained an extra methylene in the valeric acid chain of biotin (i.e., homobiotin), or contained conjugated amino acids having hydroxymethylene, carboxylate, or acetate functionalities on a methylene alpha to the biotinamide bond. The biotinidase hydrolysis assay was conducted on biotin derivs. that were radioiodinated at high specific activity, and then subjected to dild. human serum at 37.degree. for 2 h. After incubation, assessment of biotinamide bond hydrolysis by biotinidase was readily achieved by measuring the percentage of radioactivity that did not bind with avidin. As controls, an unsubstituted biotin deriv. which is rapidly cleaved by biotinidase and an N-methyl-substituted biotin deriv. which is stable to biotinidase cleavage were included in the study. The results indicate that increasing the distance from the biotin ring structure to the biotinamide bond by one methylene only decreases the rate of biotinidase cleavage, but does not block it. The data obtained also indicate that placing a hydroxymethylene, carboxylate, or acetate alpha to the biotinamide bond is effective in blocking the biotinamide hydrolysis reaction. These data, in combination with data previously obtained, which indicate that biotin derivs. contg. hydroxymethylene or carboxylate moieties retain the slow dissocn. rate of biotin from avidin and streptavidin [Wilbur, D. S., et al. (2000) Bioconjugate Chem. 11, 569-583], strongly support incorporation of these structural features into biotin derivs. being used for in vivo targeting applications.

IT **194920-45-1P 194920-46-2P 194920-60-0P**
194920-61-1P 194920-64-4P 194920-71-3P

351534-98-0P 351534-99-1P 351535-00-7P
351535-01-8P 351535-05-2P 351535-06-3P
RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(biotin reagents for antibody pretargeting.)
IT **351535-09-6P 351535-10-9P 351535-11-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(biotin reagents for antibody pretargeting.)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:194054 HCAPLUS
DOCUMENT NUMBER: 134:367106
TITLE: Synthesis of biotinylated bis-(D-glucose) derivatives for glucose transporter photoaffinity labeling
AUTHOR(S): Hashimoto, M.; Hatanaka, Y.; Yang, J.; Dhesi, J.; Holman, G. D.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Claverton Down, Bath, BA2 7AY, UK
SOURCE: Carbohydrate Research (2001), 331(2), 119-127
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New diazirine based bis-glucose derivs. for tagging glucose transporters have been synthesized. These included two biotinylated compds. linked either by an aminocaproate or by a cleavable dithiol link. These compds. have been derivatized via a key skeleton compd. that can be easily used for introduction of addnl. tags. Studies on the erythrocyte glucose transporter (GLUT1) and the insulin-stimulated adipose cell transporter (GLUT4) have revealed the biotinylated photoreactive bis-glucose compds. are effective labeling reagents.
IT **340293-00-7P 340293-01-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of biotinylated bisglucose derivs. for glucose transporter photoaffinity labeling)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:52907 HCAPLUS
DOCUMENT NUMBER: 134:277052
TITLE: Cell-surface recognition of biotinylated membrane proteins requires very long spacer arms: an example from glucose-transporter probes
AUTHOR(S): Hashimoto, Makoto; Yang, Jing; Holman, Geoffrey D.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK
SOURCE: ChemBioChem (2001), 2(1), 52-59
Published in: Angew. Chem., Int. Ed., 40(1)
CODEN: CBCHFX; ISSN: 1439-4227
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glucose transporters (GLUTs) can be photoaffinity labeled by

(diazirinetrifluoroethyl)benzoyl-substituted glucose derivs. and the adduct can be recognized, after detergent solubilization of membranes, by using streptavidin-based detection systems. However, in intact cells recognition of photolabeled GLUTs by avidin and anti-biotin antibodies only occurs if the bridge between the photoreactive and the biotin moieties has a min. of 60-70 spacer atoms. We show that a suitably long bridge can be synthesized with a combination of polyethylene glycol and tartrate groups and that introduction of these spacers generates hydrophilic products that can be cleaved with periodate. Introduction of the very long spacers does not appreciably reduce the affinity of interaction of the probes with the transport system.

IT **332941-45-4P 332941-49-8P 332941-52-3P**
332941-54-5P 332941-56-7P
RL: PNU (Preparation, unclassified); RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(reagents with long spacer arms between biotin and photoaffinity label can be used for cell-surface recognition of biotinylated glucose transporters)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:895537 HCAPLUS
DOCUMENT NUMBER: 134:204239
TITLE: Development of Biotin-Avidin Technology to Investigate Okadaic Acid-Promoted Cell Signaling Pathway
AUTHOR(S): Konoki, K.; Sugiyama, N.; Murata, M.; Tachibana, K.; Hatanaka, Y.
CORPORATE SOURCE: Department of Chemistry, School of Science, The University of Tokyo, Tokyo, Bunkyo-Ku, Hongo, 113-0033, Japan
SOURCE: Tetrahedron (2000), 56(46), 9003-9014
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:204239

AB Four biotin conjugates of okadaic acid were synthesized for evaluating their interactions with protein phosphatase 2A (PP2A) by surface plasmon resonance (SPR). C7-biotinylated okadaic acid exhibited the strongest binding affinity to the enzyme, while C1-biotinylated deriv. was devoid of affinity. C24- or C27-biotinylated okadaic acid showed moderate affinity to the enzyme. In the wake of this finding, a biotinyl photoaffinity probe was introduced into 7-OH of okadaic acid. Photoaffinity labeling followed by SDS-PAGE anal. indicated that the okadaic acid deriv. clearly labeled PP2A. Furthermore, three proteins were also labeled in crude exts. of a marine sponge Halichondria okadai. All these results imply that the C7-biotin conjugate is a versatile reagent for biochem. studies of okadaic acid-binding proteins including PP2A.

IT **328273-51-4P**
RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(development of biotin-avidin technol. to investigate okadaic acid-promoted cell signaling pathway)

IT **328273-42-3P 328273-45-6P 328273-48-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(development of biotin-avidin technol. to investigate okadaic acid-promoted cell signaling pathway)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:861452 HCAPLUS
DOCUMENT NUMBER: 134:29252
TITLE: Synthesis of water soluble multi-biotin-containing compounds for use in targeting biotin-binding proteins
PATENT ASSIGNEE(S): University of Washington, USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072802	A2	20001207	WO 2000-US15081	20000601
WO 2000072802	A3	20020207		
W: AU, BR, CA, IL, JP, KR, MX, RU				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1196199	A2	20020417	EP 2000-938025	20000601
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1999-324267 A 19990602
WO 2000-US15081 W 20000601

AB Syntheses of water sol. discrete multi-biotin-contg. compds. with at least three biotin moieties are disclosed. The water sol. biotin-contg. compds. may addnl. comprise one or more moieties that confer resistance to cleavage by biotinidase or that is cleavable in vitro or in vivo. The discrete multi-biotin-contg. compds. may include a reactive moiety that provides a site for reaction with yet another moiety, such as a targeting, diagnostic or therapeutic functional moiety. Biotinylation reagents comprising water sol. linker moieties are also disclosed and may addnl. comprise a biotinidase protective group. Methods for amplifying the no. of sites for binding biotin-binding proteins at a selected target using multi-biotin compds. are also disclosed.

IT **194920-56-4P 194920-58-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis of water sol. multi-biotin-contg. compds. for use in targeting biotin-binding proteins)

L13 ANSWER 8 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:608717 HCAPLUS
DOCUMENT NUMBER: 133:207678
TITLE: Preparation of sulfonamide derivs. as amyloid .beta. production inhibitors useful in treating or preventing diseases related to A.beta.
INVENTOR(S): Smith, David W.; Munoz, Benito; Srinivasan, Kumar; Bergstrom, Carl P.; Chaturvedula, Prasad V.; Deshpande, Milind S.; Keavy, Daniel J.; Lau, Wai Yu; Parker, Michael F.; Sloan, Charles P.; Wallace, Owen B.; Wang, Henry Hui

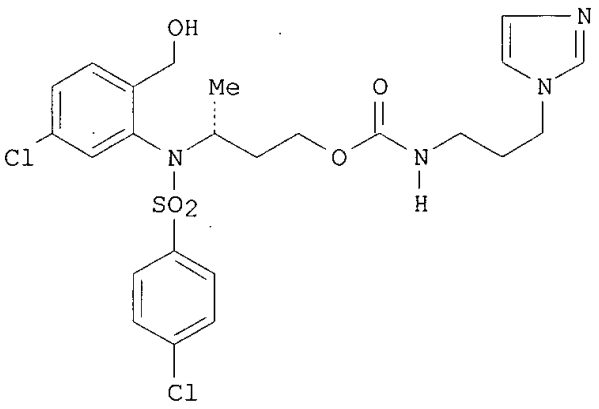
PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Bristol-Myers Squibb Company
SOURCE: PCT Int. Appl., 377 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
~~WO 2000050391~~	A1	20000831	WO 2000-US4560	20000222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1159263	A1	20011205	EP 2000-910293	20000222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000008965	A	20020226	BR 2000-8965	20000222
NO 2001004135	A	20010927	NO 2001-4135	20010824

PRIORITY APPLN. INFO.:

US 1999-121906P	P	19990226
US 1999-122746P	P	19990226
US 1999-122748P	P	19990226
US 1999-130994P	P	19990423
US 1999-130995P	A2	19990423
WO 2000-US4560	W	20000222

OTHER SOURCE(S): MARPAT 133:207678
GI



I

AB Title compds. [(D)(G)CHN(E)SO2(J); D = H, alkyl, heterocycle, halo, alkoxyl, ester, amide; G = alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, cycloalkynyl, (CHR1)nO(CHR2)mCONR3R4, heterocycle, aryl, amine, amide, ester, ether, carbamate; D-G = cyclic; n = 1, 2, 3, 4; m = 0, 1, 2, 3, 4; R1, R2, R3, R4 are independently H, alkyl; R3-R4 = cyclic; E = H, alkyl, alkenyl, alkynyl, heterocycle, aryl, alkoxyl, amide, sulfonyl, sulfonamidyl, sulfide; J = alkyl, alkenyl, alkynyl, aryl,

heterocycle, polycyclic; J-E = cyclic], pharmaceutically acceptable salts, and compn. comprising title compds. are prepd. Title compds. can act to modulate prodn. of amyloid .beta. protein (APP751, APP695wt, APP670/671, APP670/671/717, sAPP, .alpha.-sAPP, .beta.-sAPP) and are useful in the prevention or treatment of a variety of diseases; such diseases are amyloid angiopathy, cerebral amyloid angiopathy, systemic amyloidosis, Alzheimer's disease, hereditary cerebral hemorrhage with amyloidosis of the Dutch type, inclusion body myositis, and Down's syndrome. Thus, the title compd. I was prepd. and tested.

IT **290330-19-7P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of sulfonamide derivs. as amyloid .beta. prodn. inhibitors useful in treating or preventing diseases related to A.beta.)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 9 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:550007 HCAPLUS
DOCUMENT NUMBER: 134:2118
TITLE: Development of biotin trimers as reagents to increase (radio)nuclide localization in antibody pretargeting
AUTHOR(S): Wilbur, D. S.; Pathare, P. M.; Hamlin, D. K.; Stayton, P. S.; Klumb, L. A.; Tan, P.; To, R.; Buhler, K. R.; Vessella, R. L.
CORPORATE SOURCE: Departments of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds 1997, Proceedings of the International Symposium, 6th, Philadelphia, PA, United States, Sept. 14-18, 1997 (1998), Meeting Date 1997, 295-298. Editor(s): Heys, J. Richard; Melillo, David G. John Wiley & Sons Ltd.: Chichester, UK.
CODEN: 69AGFQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The authors provide a method of prepg. compds. which contain three biotin moieties and an arylstannane moiety for application to tumor pretargeting of radionuclides.
IT **308831-29-0P 308831-30-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(development of biotin trimers as reagents to increase radionuclide localization in antibody pretargeting)
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:475784 HCAPLUS
DOCUMENT NUMBER: 133:100420
TITLE: Optical sorting method applied to in vitro evolution
INVENTOR(S): Griffiths, Andrew; Tawfik, Dan
PATENT ASSIGNEE(S): Medical Research Council, UK
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040712	A1	20000713	WO 2000-GB30	20000106
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141272	A1	20011010	EP 2000-900080	20000106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: GB 1999-298 A 19990107
WO 2000-GB30 W 20000106

AB The invention describes a method for isolating one or more genetic elements encoding a gene product having a desired activity, comprising the steps of: (a) compartmentalizing genetic elements into microcapsules; (b) expressing the genetic elements to produce their resp. gene products within the microcapsules; (c) sorting the genetic elements which produce the gene product having the desired activity using a change in the optical properties of the microcapsule contents. The invention enables the in vitro evolution of nucleic acids and proteins by repeated mutagenesis and iterative applications of the method of the invention. Thus, a caged, biotin-labeled glutathione-S-transferase substrate was synthesized. Water-in-oil emulsions contg. this enzyme along with the substrate and 2,4-dinitrochlorobenzene demonstrated that the gene for the enzyme could be expressed in this system and that the enzyme produced could create a fluorescent product from the caged, biotin-labeled substrate and 2,4-dinitrochlorobenzene. The product was uncaged by UV irradn. then captured on avidin-coated beads. The product-coated beads were detected by flow cytometry. A complementary expt. demonstrated the expression of the GFP gene in this water-in-oil emulsion system.

IT **282718-77-8P 282718-82-5P**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(optical sorting method applied to in vitro evolution)

IT **282718-83-6P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(optical sorting method applied to in vitro evolution)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 11 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:431259 HCAPLUS
DOCUMENT NUMBER: 133:208058
TITLE: A trifunctional reagent for photoaffinity labeling
AUTHOR(S): Ruhl, Thomas; Hennig, Lothar; Hatanaka, Yasumaru; Burger, Klaus; Welzel, Peter
CORPORATE SOURCE: Universitat Leipzig, Institut fur Organische Chemie, Leipzig, D-04103, Germany
SOURCE: Tetrahedron Letters (2000), 41(23), 4555-4558
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:208058
AB A photolabel, a biotin tag, and a moenomycin ligand were attached orthogonally to the 3 functional groups of isoserine to provide a compd. (I) that is to be used in affinity labeling of penicillin-binding protein. The urethane group in I is cleaved with BuNH2 in MeOH or H2O.
IT **290812-04-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of photolabel for affinity labeling of penicillin-binding protein)
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 12 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:35037 HCAPLUS
DOCUMENT NUMBER: 132:90367
TITLE: Trifunctional reagent for conjugation to a biomolecule for use in diagnosis and therapy
INVENTOR(S): Wilbur, D. Scott; Sandberg, Bengt E. B.
PATENT ASSIGNEE(S): Dept. of Radiation Oncology, University of Washington, USA; Mitra Medical Technology AB
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002051	A1	20000113	WO 1999-SE1241	19990707
W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9950767	A1	20000124	AU 1999-50767	19990707
EP 1095274	A1	20010502	EP 1999-935251	19990707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001023288	A1	20010920	US 2000-750280	20001229
NO 2001000021	A	20010307	NO 2001-21	20010103

PRIORITY APPLN. INFO.:
SE 1998-1345 A 19980707
WO 1998-SE1345 A 19980707
WO 1999-SE1241 W 19990707

AB A reagent for conjugation to a biomol. for diagnosis and treatment of human and animal conditions and diseases is described, wherein the reagent is a single mol. with at least three functional parts and a) wherein a trifunctional crosslinking moiety is coupled to b) an affinity ligand via a linker 1, said affinity ligand being capable of binding with another mol. having affinity for said ligand; to c) an effector agent, optionally via a linker 2, said effector agent exerting its effects on cells, tissues and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive moiety, optionally via a linker 3, said moiety being capable of forming a

bond between the reagent and the biomol. The affinity ligand is esp. biotin or a biotin deriv. The effector agent is a toxin, an enzyme capable of converting a prodrug to an active drug, an immunosuppressant, an immunostimulant, or a radionuclide-binding agent, with or without the radionuclide.

IT **254441-23-1 254441-24-2D**, derivs. **254441-25-3 254441-26-4 254441-28-6 254447-29-5 254447-31-9**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 13 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:35036 HCAPLUS
DOCUMENT NUMBER: 132:90366
TITLE: Trifunctional reagent for conjugation to a biomolecule for use in diagnosis and therapy
INVENTOR(S): Wilbur, D. Scott; Sandberg, Bengt E. B.
PATENT ASSIGNEE(S): Department of Radiation Oncology, University of Washington, USA; Mitra Medical Technology AB
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002050	A1	20000113	WO 1998-SE1345	19980707
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9883663	A1	20000124	AU 1998-83663	19980707
AU 9950767	A1	20000124	AU 1999-50767	19990707
EP 1095274	A1	20010502	EP 1999-935251	19990707
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001000021	A	20010307	NO 2001-21	20010103

PRIORITY APPLN. INFO.: WO 1998-SE1345 A 19980707
WO 1999-SE1241 W 19990707

AB A reagent for conjugation to a biomol. for diagnosis and treatment of human and animal conditions and diseases is described, wherein the reagent is a single mol. with at least three functional parts and a) wherein a trifunctional crosslinking moiety is coupled to b) an affinity ligand via a linker 1, said affinity ligand being capable of binding with another mol. having affinity for said ligand; to c) an effector agent, optionally via a linker 2, said effector agent exerting its effects on cells, tissues

and/or humorous mols. in vivo or ex vivo; and to d) a biomol. reactive moiety, optionally via a linker 3, said moiety being capable of forming a bond between the reagent and the biomol. The affinity ligand is esp. biotin or a biotin deriv. The effector agent is a toxin, an enzyme capable of converting a prodrug to an active drug, an immunosuppressant, an immunostimulant, or a radionuclide-binding agent, with or without the radionuclide.

IT **254441-23-1 254441-24-2D**, derivs. **254441-25-3 254441-26-4 254441-28-6 254447-29-5**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent); USES (Uses)
(trifunctional reagent for conjugation to a biomol. for use in diagnosis and therapy)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 14 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:753428 HCAPLUS
DOCUMENT NUMBER: 132:1814
TITLE: Bis-biotin compounds for specific binding assays
INVENTOR(S): Pirio, Marcel Rene; Davalian, Dariush; Ishkanian, Jacqueline Sadakan; Ullman, Edwin F.
PATENT ASSIGNEE(S): Dade Behring Inc., USA
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9960400	A1	19991125	WO 1999-US10960	19990519
W: JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6153442	A	20001128	US 1998-81873	19980520
EP 1005650	A1	20000607	EP 1999-923193	19990519
R: CH, DE, ES, FR, GB, IT, LI, NL, SE				

PRIORITY APPLN. INFO.: US 1998-81873 A 19980520
WO 1999-US10960 W 19990519

AB The present invention relates to compds. that are bis-biotins. These compds. comprise two biotinyl radicals connected by a chain of atoms, usually at least 16 atoms in length. The bis-biotin is conjugated to a member of a specific binding pair ("sbp member") wherein the chain is not part of the sbp member. Also disclosed are compns. comprising a complex of avidin and a bis-biotin as described above. The compds. and compns. of the invention find use in an assay for an analyte wherein there is employed a reagent system comprising an avidin reagent and a biotin reagent. The improvement of the present invention comprises using as the biotin reagent a bis-biotin as described above. Also disclosed are kits comprising the present bis-biotins and methods of prepg. a bis-biotinylated conjugate of a member of a specific binding pair ("sbp member") for use in a specific binding assay. A bis-biotin conjugate with digoxin was prepd. and complexed with sensitizer beads having immobilized streptavidin. The beads were used in a chemiluminescence immunoassay for digoxin.

IT **251096-25-0DP**, complexes with streptavidin-sensitizer beads
RL: ARG (Analytical reagent use); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(for digoxin assay, stability of; bis-biotin compds. for specific binding assays)
IT **251096-26-1DP**, complexes with streptavidin-sensitizer beads
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(for thyroxine assay; bis-biotin compds. for specific binding assays)
IT **251096-25-0P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in prepn. of digoxin assay reagent; bis-biotin compds. for specific binding assays)
IT **251096-24-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in prepn. of digoxin assay reagent; bis-biotin compds. for specific binding assays)
IT **251096-26-1DP**, complexes with streptavidin-sensitizer beads
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in prepn. of thyroxine assay reagent; bis-biotin compds. for specific binding assays)
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 15 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:313314 HCAPLUS
DOCUMENT NUMBER: 131:110893
TITLE: Functionalized Congeners of 1,4-Dihydropyridines as Antagonist Molecular Probes for A3 Adenosine Receptors
AUTHOR(S): Li, An-Hu; Chang, Louis; Ji, Xiao-duo; Melman, Neli; Jacobson, Kenneth A.
CORPORATE SOURCE: Molecular Recognition Section Laboratory of Bioorganic Chemistry, National Institute of Diabetes Digestive and Kidney Diseases National Institutes of Health, Bethesda, MD, 20892-0810, USA
SOURCE: Bioconjugate Chemistry (1999), 10(4), 667-677
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 4-Phenylethynyl-6-phenyl-1,4-dihydropyridine derivs. are selective antagonists at human A3 adenosine receptors, with Ki values in a radioligand binding assay vs. [125I]AB-MECA [N6-(4-amino-3-iodobenzyl)-5'-N-methylcarbamoyl-adenosine] in the submicromolar range. In this study, functionalized congeners of 1,4-dihydropyridines were designed as chem. reactive adenosine A3 antagonists, for the purpose of synthesizing mol. probes for this receptor subtype. Selectivity of the new analogs for cloned human A3 adenosine receptors was detd. in radioligand binding in comparison to binding at rat brain A1 and A2A receptors. Benzyl ester groups at the 3- and/or 5-positions and Ph groups at the 2- and/or 6-positions were introduced as potential sites for chain attachment. Structure-activity anal. at A3 adenosine receptors indicated that 3,5-dibenzyl esters, but not 2,6-di-Ph groups, are tolerated in binding. Ring substitution of the 5-benzyl ester with a 4-fluorosulfonyl group provided enhanced A3 receptor affinity resulting in a Ki value of 2.42 nM; however, a long-chain deriv. contg. terminal amine functionalization at

the 4-position of the 5-benzyl ester showed only moderate affinity. This sulfonyl fluoride deriv. appeared to bind irreversibly to the human A3 receptor (1 h incubation at 100 nM resulting in the loss of 56% of the specific radioligand binding sites), while the binding of other potent dihydropyridines and other antagonists was generally reversible. At the 3-position of the dihydropyridine ring, an amine-functionalized chain attached at the 4-position of a benzyl ester provided higher A3 receptor affinity than the corresponding 5-position isomer. This amine congener was also used as an intermediate in the synthesis of a biotin conjugate, which bound to A3 receptors with a Ki value of 0.60 .mu.M.

IT **233265-81-1P**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(dihydropyridine functionalized congener prepn. as antagonist mol. probes for A3 adenosine receptors)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:776598 HCAPLUS
DOCUMENT NUMBER: 130:38641
TITLE: Preparation of water soluble vitamin B12 as antiinflammatory receptor modulating agents
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington
SOURCE: U.S., 66 pp., Cont.-in-part of U.S. Ser. No. 406,191.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5840712	A	19981124	US 1995-545151	19951019
US 5739287	A	19980414	US 1995-406192	19950316
US 5840880	A	19981124	US 1995-406191	19950316
US 5869465	A	19990209	US 1995-406194	19950316
WO 9714711	A1	19970424	WO 1996-US16672	19961018
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9677182	A1	19970507	AU 1996-77182	19961018
EP 1015475	A1	20000705	EP 1996-940247	19961018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6083926	A	20000704	US 1998-200422	19981123

PRIORITY APPLN. INFO.:
US 1994-224831 B2 19940408
US 1995-406191 A2 19950316
US 1995-406192 A2 19950316
US 1995-406194 A2 19950316
WO 1995-US4404 A2 19950407
US 1995-545151 A 19951019

US 1995-545496 A 19951019
WO 1996-US16672 W 19961018
OTHER SOURCE(S): MARPAT 130:38641
AB Vitamin B12 antiinflammatory receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker. Synthesis of a vitamin B12/biotin conjugate and fusion protein receptor modulating agent is reported.
IT **189887-16-9P 189887-17-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of water sol. vitamin B12 as antiinflammatory receptor modulating agents)
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 17 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:266383 HCAPLUS
DOCUMENT NUMBER: 129:119561
TITLE: Photocrosslinking as an approach to structural biology: structural analysis of .beta.1,4-galactosyltransferase
AUTHOR(S): Hatanaka, Yasumaru; Hashimoto, Makoto; Kanaoka, Yuichi
CORPORATE SOURCE: Research Institute for Wakan-Yaku, Toyama Medical and Pharmaceutical University, Toyama, 930-01, Japan
SOURCE: Photomed. Photobiol. (1997), 19, 83-84
CODEN: PHPHEA; ISSN: 0912-232X
PUBLISHER: Japanese Society for Photomedicine and Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel photochem. crosslinking reagent, N-[2-[2-[2-(2-biotinylaminoethoxy)-ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]-benzoyl]-N4-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-L-aspartamide (BDGA), was applied for the anal. of acceptor binding-site within .beta.1,4-galactosyltransferase (GalT). Using this carbene-generating N-acetylglucosamine deriv., a biotin tag was specifically introduced at the acceptor substrate binding-site of GalT. The biotin tag photochem. attached on GalT protein harness the power of avidin-biotin technol. for the high-sensitive detection and one-step purifn. of photolabeled GalT protein. Thus, we have examd. an efficient strategy for the localization of photolabeled site by using a chemiluminescent technique for the radioisotope free detection trace amt. of labeled products and an immobilized avidin for the selective retrieval of biotinylated components. Our approach successfully identified photolabeled fragments corresponding to the GalT acceptor substrate region where is no predictable sequence from the homol. search. The results clearly demonstrate that the biotinylation using BDGA could provide efficient methods' for the structural biol. of glycosyltransferases which shares no significant sequential homol. or is difficult to crystallize.
IT **186263-07-0**, BDGA
RL: RCT (Reactant)
(photocrosslinking in structural anal. of .beta.1,4-galactosyltransferase)

L13 ANSWER 18 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:223967 HCAPLUS

DOCUMENT NUMBER: 129:25290
TITLE: Cell-surface biotinylation of GLUT4 using bis-mannose photolabels
AUTHOR(S): Koumanov, Francoise; Yang, Jing; Jones, Alison E.; Hatanaka, Yasumaru; Holman, Geoffrey D.
CORPORATE SOURCE: Department of Biology and Biochemistry, University of Bath, Bath, BA2 7AY, UK
SOURCE: Biochemical Journal (1998), 330(3), 1209-1215
CODEN: BIJOAK; ISSN: 0264-6021
PUBLISHER: Portland Press Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB New cell-impermeant bis-mannose photolabels were developed with biotinyl groups attached to 4-(I-azi-2,2,2-trifluoroethyl)-benzoyl-1,3-bis(D-mannos-4-yloxy)-2-propylamine (ATB-BMPA) by either a polyethoxy spacer (Bio-ATB-BMPA) or an addnl. hexanoic acid spacer (Bio-LC-ATB-BMPA). The half-maximal inhibition consts., Kl values, for inhibition of glucose transport activity in insulin-stimulated rat adipocytes were detd. to be 359 and 273 .mu.M for Bio-ATB-BMPA and Bio-LC-ATB-BMPA, resp. These values are similar to those previously reported for the non-biotinylated compd. ATB-BMPA. Following UV-irradn.-induced crosslinking of the biotinylated photolabels to rat adipocytes, the biotinylated glucose transporter isoform 4 (GLUT4) was detected by non-radioactive and radioactive methods that utilized the interaction with streptavidin. Biotinylated GLUT4 from 1-2 .mu.g of adipose cell membranes, pptd. onto magnetic streptavidin beads, could be sensitively and quant. detected using an electrochemiluminescent assay method. This utilized a ruthenium-tagged anti-GLUT4 antibody that on excitation at an electrode generated an electrochemiluminescent signal in an ORIGEN analyzer. Alternatively, surface-biotinylated GLUT4 could be easily, but less sensitively, detected in streptavidin agarose ppts. which were analyzed by conventional GLUT4 Western blotting. Data obtained using the non-radioactive methods compared favorably with those using tritiated versions of the biotinylated probes. Insulin treatment of adipocytes increased the levels of signals from surface biotinylated GLUT4 by .apprx. 10-fold or .apprx. 20-fold, resp., when the electrochemiluminescent or the Western blot detection methods were used and these signals were blocked by cytochalasin B.

IT **207971-24-2P 207971-25-3P**
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(cell-surface biotinylation of GLUT4 using bis-mannose photolabels)

L13 ANSWER 19 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:52144 HCAPLUS
DOCUMENT NUMBER: 128:72612
TITLE: A Rapid and Efficient Method for Identifying Photoaffinity Biotinylated Sites within Proteins
AUTHOR(S): Hatanaka, Yasumaru; Hashimoto, Makoto; Kanaoka, Yuichi
CORPORATE SOURCE: Research Institute for Wakan-yaku, Toyama Medical and Pharmaceutical University, Sugitani, 2630, Japan
SOURCE: J. Am. Chem. Soc. (1998), 120(2), 453-454
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rapid and efficient strategy has been developed for identification of photoaffinity labeled peptides. The strategy involves a radioisotope-free approach in which the photoaffinity label is biotinylated. The method

then utilizes a novel derivatization of PVDF membrane for identification and anal. of peptide fragments derived from the photoaffinity labeled binding site in a simple dot blot assay. In the present study, the method has been applied to identification of the binding site region of .beta.1,4-galactosyltransferase (galT). Sequence anal. has revealed that the biotinylated photoprobe is localized in a tryptic GalT fragment (Y197-R208). These data are consistent with previous suggestions concerning the GalT acceptor site and clearly demonstrate the effectiveness of our approach for rapid identification of photolabeled peptides.

IT **186263-07-0**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(a rapid and efficient method for identifying photoaffinity biotinylated sites within proteins)

L13 ANSWER 20 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:708440 HCAPLUS
DOCUMENT NUMBER: 127:298612
TITLE: Biotin Reagents for Antibody Pretargeting. 2. Synthesis and in Vitro Evaluation of Biotin Dimers and Trimers for Crosslinking of Streptavidin
AUTHOR(S): Wilbur, D. Scott; Pathare, Pradip M.; Hamlin, Donald K.; Weerawarna, S. Ananda
CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chem. (1997), 8(6), 819-832
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polymn. and/or crosslinking of recombinant streptavidin (r-SAv) with biotin derivs. contg. two biotin moieties (biotin dimers) or three biotin moieties (biotin trimers) has been investigated as a model for reagents to be used to increase the amt. of radioactivity on cancer cells in tumor pretargeting protocols. In the investigation, six biotin dimers and three biotin trimers were synthesized. Most biotin derivs. synthesized had ether contg. linker mols. incorporated to improve their aq. soly. The synthesized biotin dimers contained linker moieties which provided distances (when fully extended) of 13-49 .ANG. between biotin carboxylate carbon atoms, and the biotin trimers contained linker moieties which provided distances of 31-53 .ANG. between any two biotin carboxylate atoms. All of the biotin derivs. were evaluated for their ability to polymerize r-SAv in soln. When the biotin derivs. were mixed with r-SAv, none of the biotin dimers caused polymn., but all of the biotin trimers resulted in complete polymn. Some of the biotin dimers did cross-link r-SAv (to form r-SAv dimers, trimers, etc.), but the percentage of crosslinking was low (.ltoreq.40%). The length of the linker mol. was important in crosslinking of biotin dimers. While linkers which provided distances of 13 and 19 .ANG. between biotin carboxylate carbon atoms did not result in crosslinking, a linker which provided a 17 .ANG. distance resulted in a small (.ltoreq.10%) amt. of crosslinking. Also, crosslinking was increased in biotin dimers with linkers which provided distances between biotin carboxylate carbon atoms of .gtoreq.23 .ANG.. Crosslinking of streptavidin bound in polystyrene wells with biotin dimers and trimers was also examd. In those expts., an excess of each biotin deriv. was incubated at 37 .degree.C for 10-30 min in polystyrene wells contg. bound SAv. After the excess biotin deriv. was rinsed from the wells, an excess of r-[125I]SAv was incubated for another 10-30 min. The amt. of r-[125I]SAv bound after rinsing the excess from the wells was an

indicator of the extent of crosslinking that occurred. The process of alternating addns. of reagents was repeated four times to demonstrate that bound radioactivity could be increased with each addn. of [125I]SAv. The results of crosslinking r-SAv in polystyrene wells paralleled results from crosslinking in soln.

IT **194920-45-1P 194920-46-2P 194920-56-4P**
194920-58-6P 194920-64-4P 195370-62-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and in vitro evaluation of biotin dimers and trimers for crosslinking of streptavidin)

L13 ANSWER 21 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:542454 HCAPLUS
DOCUMENT NUMBER: 127:220519
TITLE: Preparation of biotin containing compounds with water soluble linker moieties for use as radionuclides and streptavidin crosslinking agents
INVENTOR(S): Wilbur, Scott D.; Pathare, Pradip M.; Weerawarna, S. Ananda; Hamlin, Donald K.
PATENT ASSIGNEE(S): Board of Regents of the University of Washington, USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9729114	A1	19970814	WO 1997-US2560	19970207
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9720524	A1	19970828	AU 1997-20524	19970207

PRIORITY APPLN. INFO.: US 1996-11321P P 19960208
WO 1997-US2560 W 19970207

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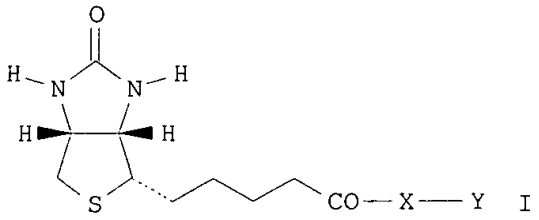
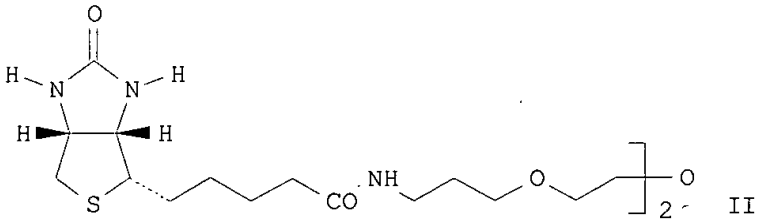




AB Water sol. biotin-contg. compds. and biotinylation reagents I {X = divalent water sol. linker such as NH(CH2)3O(CH2)2O(CH2)2O(CH2)3NH, trivalent water sol. linker such as 1,3,5-C6H3[CONH(CH2)3O(CH2)2O(CH2)2O(CH2)3NH]3; Y = reactive moiety such as 4-Bu3Sn-C6H4-CO; targeting, diagnostic, or therapeutic moiety such as 4-125I-C6H4-CO, biotin, or cyano-e-cobalamin} were prepd. for use as biotinylation reagents, biotinidase inhibitors (no data), and streptavidin cross linking agents. Thus, biotin dimer II was prepd. starting from biotin and 4,7,10-trioxa-1,13-tridecanediamine and was tested for streptavidin cross linking.

IT **194920-56-4P 194920-58-6P 194920-60-0P 194920-61-1P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biotin contg. compds. with water sol. linker moieties for use as biotinylation reagents, radionuclides, biotinidase inhibitors, and streptavidin crosslinking agents)

IT **194920-64-4P 194920-71-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of biotin contg. compds. with water sol. linker moieties for use as biotinylation reagents, radionuclides, biotinidase inhibitors, and streptavidin crosslinking agents)

IT **194920-45-1P 194920-46-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of biotin contg. compds. with water sol. linker moieties for use as biotinylation reagents, radionuclides, biotinidase inhibitors, and streptavidin crosslinking agents)

L13 ANSWER 22 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433652 HCAPLUS
DOCUMENT NUMBER: 127:121587
TITLE: Biotin reagents for antibody pretargeting. Synthesis, radioiodination and in vitro evaluation of water soluble, biotinidase resistant biotin derivatives
AUTHOR(S): Wilbur, D. Scott; Hamlin, Donald K.; Pathare, Pradip M.; Weerawarna, S. Ananda

CORPORATE SOURCE: Department of Radiation Oncology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Bioconjugate Chem. (1997), 8(4), 572-584
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB An investigation was conducted to examine the stability of water solubilized, radioiodinated biotin derivs. toward biotinidase degrdn. in mouse and human serum as development of antibody pretargeting for cancer therapy. Eight new biotin derivs. were synthesized to conduct the study. The biotin derivs. synthesized contained (1) the biotin moiety, (2) a water solubilizing linker moiety, (3) p-iodobenzoate or p-tributylstannylbenzoate moieties, and (4) in some compds., N-Me or .alpha.-Me contg. moieties were added to block biotinidase activity. The linker moiety, 4,7,10-trioxa-1,13-tridecanediamine was included in the biotin derivs. to improve their water soly., and functioned as a 17 .ANG. spacer between the biotin and benzoyl moieties. Four of the new p-tributylstannylbenzoyl biotin derivs. I (R = H, Me; X = SnBu3), II (X = SnBu3), III (X = SnBu3) could be radioiodinated in the last synthetic step. The other four p-iodobenzoyl biotin derivs. I (R = H, Me; X = I), II (X = I), III (X = I) were used as HPLC ref. stds. Initial studies involved radioiodination of I (R = H; X = SnBu3) to yield [125I]-I (R = H; X = 125I). Radioiodinated I (R = H; X = I), did not contain a moiety for blocking biotinidase activity and was found to be rapidly degraded in both mouse and human serum at 37 .degree.C. Derivs. designed to be stable to biotinidase incorporated N-Me and .alpha.-Me moieties adjacent to the biotin carboxylate group. Linkers in the biotin derivs. were 4,7,10-trioxa-1,13-tridecanediamine, its N,N-di-Me analog or sarcosine (N-methylglycine). The radioiodinated N-Me contg. biotin derivs. I (R = Me; X = 125I) and II (X = 125I) were very stable to biotinidase degrdn. The radioiodinated .alpha.-Me contg. deriv., III (X = 125I), has an intermediate stability with regards to biotinidase degrdn.

IT **192720-95-9P 192720-97-1P 192720-99-3P**
192721-01-0P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis, radioiodination and in vitro evaluation of water sol., biotinidase resistant biotin derivs.)

IT **192720-64-2P 192720-67-5P 192720-83-5P**
192720-85-7P 192720-86-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis, radioiodination and in vitro evaluation of water sol., biotinidase resistant biotin derivs.)

IT **192720-66-4P 192720-70-0P 192720-88-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis, radioiodination and in vitro evaluation of water sol., biotinidase resistant biotin derivs.)

L13 ANSWER 23 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433600 HCAPLUS
DOCUMENT NUMBER: 127:106189

TITLE: Biotin-Pyrene Conjugates with Poly(ethylene glycol) Spacers Are Convenient Fluorescent Probes for Avidin and Streptavidin
AUTHOR(S): Marek, Markus; Kaiser, Karl; Gruber, Hermann J.
CORPORATE SOURCE: Institute of Biophysics, J. Kepler University, Linz, A-4040, Austria
SOURCE: Bioconjugate Chem. (1997), 8(4), 560-566
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conventional biotin-fluorophore conjugates with .ltoreq.14 atom spacers are strongly quenched when bound to avidin or streptavidin, whereas fluorescence becomes insensitive to receptor binding if typical fluorophores are linked to biotin via poly(ethylene glycol) (PEG) chains. In the present study the antagonism between PEG-PEG repulsion and fluorophore interaction was examd. more closely, using biotin-PEG-pyrene conjugates as model compds. The antagonistic tendencies between hydrophilic PEG chains and hydrophobic pyrene labels were about balanced in the PEG1900 deriv. since quenching was .apprx.50% in 4:1 complexes with avidin or streptavidin. In contrast, strong quenching and concomitant excimer fluorescence was seen with the biotin-PEG800-pyrene conjugate, providing for a new fluorescence assay to accurately measure avidin and streptavidin concns. at .gtoreq.40 and .gtoreq.10 nM, resp. Assocn./dissocn. kinetics were analyzed from pyrene fluorescence changes, and dissocn. consts. were deduced. About 3-fold affinities were obsd. for streptavidin as compared to avidin, and little influence of PEG chain length was seen. All affinities were increased by a factor of .apprx.3 when biotin-PEG-tetramethylrhodamine conjugates were used. The obsd. effect of fluorophore variation upon biotin binding is unexpectedly small; thus, the kinetic/thermodn. data appear to be representative for biotin-PEG conjugates in general.

IT **192432-17-0**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(biotin-pyrene conjugates with poly(ethylene glycol) spacers are convenient fluorescent probes for avidin and streptavidin)

IT **192432-86-3P**
RL: ARU (Analytical role, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(biotin-pyrene conjugates with poly(ethylene glycol) spacers are convenient fluorescent probes for avidin and streptavidin)

L13 ANSWER 24 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:433599 HCAPLUS
DOCUMENT NUMBER: 127:106188
TITLE: Biotin-Fluorophore Conjugates with Poly(ethylene glycol) Spacers Retain Intense Fluorescence after Binding to Avidin and Streptavidin
AUTHOR(S): Gruber, Hermann J.; Marek, Markus; Schindler, Hansgeorg; Kaiser, Karl
CORPORATE SOURCE: Institute of Biophysics, J. Kepler University, Linz, A-4040, Austria
SOURCE: Bioconjugate Chem. (1997), 8(4), 552-559
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Conventional biotin-fluorophore conjugates with .ltoreq.14 atom spacers lose most of their fluorescence when binding to avidin or streptavidin, as

is demonstrated in the present study. This explains the unusual fact that only biotinylated marker enzymes, but not fluorescent biotins, are regularly used in bioanalytic assays. Novel biotin-spacer-fluorophore conjugates are presented that retain intense fluorescence when binding to avidin or streptavidin. Preservation of fluorescence depends upon the use of poly(ethylene glycol) (PEG) spacers, which are shown not to interfere with biotin function. The obsd. absence of nonspecific interactions may also be attributed to the PEG chain. These novel fluorescent biotins are expected to be excellent new tools in fluorescence microscopy and related techniques.

IT **192432-17-0P 192432-19-2P**
RL: ARU (Analytical role, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
(biotin-fluorophore conjugates with poly(ethylene glycol) spacers retain intense fluorescence after binding to avidin and streptavidin)

IT **192432-16-9**
RL: RCT (Reactant)
(biotin-fluorophore conjugates with poly(ethylene glycol) spacers retain intense fluorescence after binding to avidin and streptavidin)

L13 ANSWER 25 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:377886 HCAPLUS
DOCUMENT NUMBER: 126:343813
TITLE: Preparation of vitamin B12 receptor modulating agents
INVENTOR(S): Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip M.
PATENT ASSIGNEE(S): Receptagen Corporation, USA; University of Washington; Morgan, A. Charles, Jr.; Wilbur, D. Scott; Pathare, Pradip, M.
SOURCE: PCT Int. Appl., 97 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9714711	A1	19970424	WO 1996-US16672	19961018
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
US 5840712	A	19981124	US 1995-545151	19951019
AU 9677182	A1	19970507	AU 1996-77182	19961018
EP 1015475	A1	20000705	EP 1996-940247	19961018
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
US 1995-545151 A 19951019
US 1995-545496 A 19951019
US 1994-224831 B2 19940408
US 1995-406191 A2 19950316
US 1995-406192 A2 19950316
US 1995-406194 A2 19950316
WO 1996-US16672 W 19961018

OTHER SOURCE(S): MARPAT 126:343813

AB Vitamin B12 receptor modulating agents capable of modulating cell surface receptors by affecting the cell surface receptor trafficking pathway are disclosed. The vitamin B12 receptor modulating agents are comprised of a covalently bound rerouting moiety and targeting moiety linked by a water-solubilizing linker.

IT **189887-16-9P 189887-17-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antiinflammatory activity of vitamin B12 receptor modulating agents)

L13 ANSWER 26 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:243325 HCAPLUS
DOCUMENT NUMBER: 126:289755
TITLE: Photocrosslinking of .beta.1,4-galactosyltransferase
AUTHOR(S): Hatanaka, Yasumaru; Hashimoto, Makoto; Kanaoka, Yuichi
CORPORATE SOURCE: Research Institute for Wakan-Yaku, Toyama Medical and Pharmaceutical University, Toyama, 930-01, Japan
SOURCE: Photomed. Photobiol. (1996), 18, 119-120
CODEN: PHPHEA; ISSN: 0912-232X
PUBLISHER: Japanese Society for Photomedicine and Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Photochem. crosslinking reaction using a novel photoreactive N-acetylglucosamine deriv., N4-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-2-[[2-[2-[2-[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethoxy]ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-, (S)- (BDGA), was applied for the specific biotinylation of acceptor binding-site of .beta.1,4-galactsyltransferase (GalT). The introduction of BDGA for photoaffinity labeling of bovine GalT has facilitated the subsequent steps of photolabeled product anal. based on the specific manipulation of photochem. attached biotinyl residue. The quant. chemiluminescent anal. revealed a presence of progressive decrement phenomenon in the yield of specific photolabeling with lowering the incubation temp. from 37.degree. to 20.degree. or 4.degree..

IT **186263-07-0**
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(photocrosslinking of .beta.1,4-galactosyltransferase)

L13 ANSWER 27 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:747636 HCAPLUS
DOCUMENT NUMBER: 126:114867
TITLE: Synthesis and characterization of a carbene-generating biotinylated N-acetylglucosamine for photoaffinity labeling of .beta.-(1 .fwdarw. 4)-galactosyltransferase
AUTHOR(S): Hatanaka, yasumaru; Hashimoto, Makoto; Nishihara, Shoko; Narimatsu, Hisashi; Kanoaka, Yuichi
CORPORATE SOURCE: Res. Inst. Wakan-yaku, Toyama Med. Pharm. Univ., Toyama, 930-01, Japan
SOURCE: Carbohydr. Res. (1996), 294, 95-108
CODEN: CRBRAT; ISSN: 0008-6215
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A photoreactive N-acetylglucosamine deriv., N-[2-[2-[2-(2-biotinylaminoethoxy)ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]-N4-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-L-aspartamide (BDGA), was synthesized as a carbene-generating biotinylated

probe for UDP-galactose: N-acetylglucosamine .beta.-(1.fwdarw.4)-galactosyltransferase (GalT). The photoaffinity labeling expts. of bovine GalT with BDGA under various conditions were examd. based on the quant. chemiluminescent detection of the biotinyl residue which was photochem. introduced into the GalT protein. A progressive decrease in the yield of specific photolabeling was obsd. upon lowering the incubation temp. from 37.degree. to 20.degree. or 4.degree.. Using a crude protein mixt. of recombinant human GalT, a band corresponding to the glutathione S-transferase fusion GalT protein was also specifically visualized. Furthermore, combined use of BDGA photolabeling with an immobilized avidin was found to be effective for the selective retrieval of photolabeled GalT from a reaction mixt. contg. a large amt. of unlabeled GalT protein. The results obtained clearly demonstrate that the covalent biotinylation using the carbene-generating photoaffinity reagent BDGA would be useful for the anal. of acceptor substrate binding sites within the GalT protein.

IT **186263-07-0P**, BDGA
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(synthesis and characterization of a carbene-generating biotinylated N-acetylglucosamine for photoaffinity labeling of .beta.-(1 .fwdarw. 4)-galactosyltransferase)

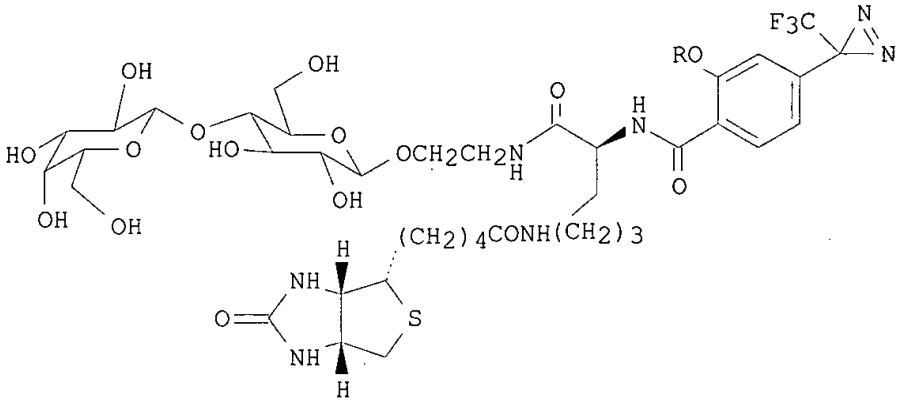
L13 ANSWER 28 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:160493 HCAPLUS
DOCUMENT NUMBER: 124:283427
TITLE: Photoaffinity labeling along with avidin-biotin system
AUTHOR(S): Hatanaka, Yasumaru; Hashimoto, Makoto; Kanaoka, Yuichi
CORPORATE SOURCE: Research Institute Wakan-Yaku, Toyama Medical and Pharmaceutical University, Toyama, 930-01, Japan
SOURCE: Photomed. Photobiol. (1995), 17, 99-100
CODEN: PHPHEA; ISSN: 0912-232X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new photoreactive N-acetylglucosamine deriv. carrying an aryl diazirine and a biotin moiety was prepd. to make use of avidin-biotin technol. for specific manipulation of photolabeled components. This reagent was applied to the photoaffinity labeling of UDP-galactose:N-acetylglucosamine .beta.-1,4-galactosyltransferase (GalT). Based on the enzyme-catalyzed signal amplification of the avidin-biotin complex, highly sensitive visualization of labeled GalT was performed by the chemiluminescent detection of the photochem. introduced biotinyl residue into the protein. Combined use of this reagent with immobilized avidin was also effective for the selective retrieval of photolabeled GalT from a reaction mixt. contg. a large amt. of unlabeled GalT protein.

IT **175663-44-2**
RL: RCT (Reactant)
(photoaffinity labeling combined with avidin-biotin for protein labeling)

L13 ANSWER 29 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:1002147 HCAPLUS
DOCUMENT NUMBER: 124:176693
TITLE: A carbene-generating biotinylated lactosylceramide analog as novel photoreactive substrate for GM3 synthase
AUTHOR(S): Hatanaka, Yasumaru; Hashimoto, Makoto; Hidari, Kazuya I.-P. Jwa; Sanai, Yutaka; Nagai, Yoshitaka; Kanaoka, Yuichi

CORPORATE SOURCE: Res. Inst. Wakan-Yaku, Toyama Medicinal and Pharmaceutical Univ., Toyama, 930-01, Japan
SOURCE: Bioorg. Med. Chem. Lett. (1995), 5(23), 2859-62
CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A new biotinylated lactose deriv. I [R = Me, 14CH3], bearing a phenyldiazirine was synthesized. A convenient approach based on avidin-biotin technol. was successfully applied for GM3 synthase assay and the Km value of this biotinylated photoprobe was detd. as 180 .mu.M using rat liver Golgi as the enzyme source. Further characterization revealed that this reagent could be a useful photoprobe for GM3 synthase.

IT **173949-62-7P 173949-63-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of a biotinylated lactosylceramide analog as substrate for GM3 synthase)

L13 ANSWER 30 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:828611 HCAPLUS
DOCUMENT NUMBER: 123:222328
TITLE: Interference-reducing agents for use in immunoassays
INVENTOR(S): Kientsch-Engel, Rosemarie; Donie, Frederic; Wiedmann, Michael
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4407423	A1	19950907	DE 1994-4407423	19940305
WO 9523800	A1	19950908	WO 1995-EP690	19950225
W: CA, CN, FI, JP, KR, US				

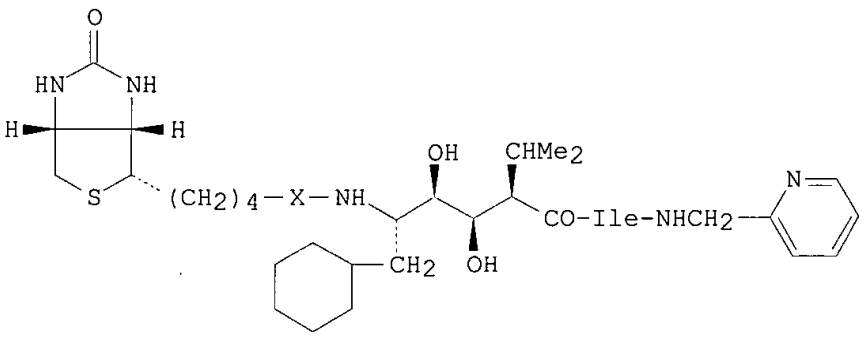
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 697021		A1	19960221	EP 1995-909783	19950225
EP 697021		B1	20000705		
	R: AT, BE, DE, DK, ES, FR, GB, GR, IE, IT, NL, PT				
JP 08508301		T2	19960903	JP 1995-522680	19950225
JP 2750003		B2	19980513		
AT 194349		E	20000715	AT 1995-909783	19950225
CA 2184386		AA	19950908	CA 1995-2184386	19950303
WO 9523801		A1	19950908	WO 1995-EP776	19950303
	W: CA, CN, FI, JP, KR, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 749435		A1	19961227	EP 1995-912194	19950303
EP 749435		B1	20001011		
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, PT, SE				
CN 1143368		A	19970219	CN 1995-191975	19950303
JP 09510289		T2	19971014	JP 1995-522705	19950303
JP 3027770		B2	20000404		
AT 196906		E	20001015	AT 1995-912194	19950303
ES 2152392		T3	20010201	ES 1995-912194	19950303
FI 9603461		A	19960904	FI 1996-3461	19960904
US 5863740		A	19990126	US 1996-700435	19960905
US 5952185		A	19990914	US 1997-958870	19971027
PRIORITY APPLN. INFO.:				DE 1994-4407423 A	19940305
				WO 1995-EP690 W	19950225
				WO 1995-EP776 W	19950303
				US 1995-535072 B1	19951103

AB The finding concerns interference-reducing agents for avoiding nonspecific reactions in immunoassays wherein the agents used are avidin or streptavidin or their derivs. Interferences in heterogeneous immunoassays can decrease sensitivity and specificity and even cause false-pos. anal. results esp. in the detn. of antibodies. The agents can be used for improving immunoassays of, e.g., haptens, antigens, or antibodies in, e.g., body fluids. Examples are given of the prepn. of, e.g., crosslinked streptavidin after activation by various crosslinking agents, of bovine serum albumin-streptavidin conjugates, etc.

IT **168411-59-4DP**, streptavidin conjugates
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(interference-reducing agents for use in immunoassays)

L13 ANSWER 31 OF 32 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1994:245753 HCAPLUS
DOCUMENT NUMBER:	120:245753
TITLE:	Evaluation of a vitamin-cloaking strategy for oligopeptide therapeutics: biotinylated HIV-1 protease inhibitors
AUTHOR(S):	Islam, I.; Ng, K. Y.; Chong, K. T.; McQuade, T. J.; Hui, J. O.; Wilkinson, K. F.; Rush, B. D.; Ruwart, M. J.; Borchardt, R. T.; Fisher, J. F.
CORPORATE SOURCE:	Upjohn Lab., Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE:	J. Med. Chem. (1994), 37(2), 293-304 CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE:	Journal
LANGUAGE:	English
GI	



I

AB A series of eight peptidic HIV-1 protease inhibitors, e.g. I [X = CO, CONH(CH2)5CO, CONH-Val, 2-CH2SC6H4CO, 2-CH2OC6H4CO], contg. the structural segment of the vitamin biotin have been prepd to address the outstanding limitations of poor oral availability and rapid biliary clearance of oligopeptide therapeutic agents. These have been evaluated with regard to the hypothesis that this vitamin would cloak the peptidic character of these oligopeptides, and thus impart to these inhibitors the potential for absorption and distribution via biotin transporters and receptors. By iterative optimization about a Cha.psi.[CH(OH)CH(OH)]Val (Cha = cyclohexylalanine) core inhibitory insert, three particularly potent inhibitors (Ki .ltoreq. 10 nM) of the HIV-1 protease were obtained. Although excellent cell culture antiviral activity is obsd. for other peptidic protease inhibitors of comparable affinity, none in this series exhibited satisfactory antiviral activity. This failure is attributed to the incompatibility of the hydrophilic and hydrogen-bonding biotin segment with the facile membrane permeability and intracellular access presumably required for antiviral activity. The ability of the biotin to cloak the peptide, and thus render the overall appearance of the conjugate as that of a vitamin, was evaluated. I [X = CO, CONH(CH2)5CO, CONH-Val, 2-CH2OC6H4CO] were evaluated for recognition by the Caco-2 cell intestinal biotin transporter. None inhibited competitively biotin uptake, indicating a lack of recognition. A vitamin may bind to a specific protein carrier, and thus attain an improved serum profile (by resistance to biliary clearance) and advantageous delivery to cells. Therefore, the serum concns. were evaluated following an i.v. bolus in a rat model for serum clearance. Protease inhibitor I (X = CONH-Val) sustained a more than 5-fold increase in serum concn. at all time points relative to the benchmark structure. The others had serum concns. at least equal to the benchmark, suggestive of improved resistance to clearance. An avidin complex of I (X = 2-CH2OC6H4CO) (II) was prepd., and its antiviral activity was identical with that of uncomplexed II. This suggests that the avidin-inhibitor complexes capable of cell internalization. Although the overall weak antiviral activity of these biotinylated inhibitors precludes consideration as practical HIV therapeutics, the overall data remain suggestive of vitamin cloaking of oligopeptides as a strategy of potential value.

IT **153805-31-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn., virucidal, and HIV protease inhibitory activity of)

L13 ANSWER 32 OF 32 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:210738 HCAPLUS
DOCUMENT NUMBER: 116:210738

TITLE: Immunochemical determination of biogenic amines
INVENTOR(S): Huber, Erasmus; Stahl, Peter; Batz, Hans Georg; Huebner-Parajsz, Christa; Jungfer, Barbara; Klein, Christian
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 25 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 471345	A1	19920219	EP 1991-113587	19910813
EP 471345	B1	19950802		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
DE 4025726	A1	19920220	DE 1990-4025726	19900814
JP 04311395	A2	19921104	JP 1991-202650	19910813

PRIORITY APPLN. INFO.: DE 1990-4025726 19900814
OTHER SOURCE(S): MARPAT 116:210738

AB A primary or secondary amine (e.g. histamine or a catecholamine) is detd. immunochem. with the aid of a monoclonal antibody produced by immortalized cells from an animal immunized with the amine conjugated, via an iso(thio)cyanato group, with a coupling agent and a carrier mol. Thus, histamine was reacted successively with (1) 3-isothiocyanatobenzoic acid, (2) N-hydroxysuccinimide and N,N'-dicyclohexylcarbodiimide, and (3) N-biotinyl-1,8-diamino-3,6-dioxaoctane. The product of synthetic step 1 was used to immunize mice, whose spleen cells were later fused with myeloma cells to provide hybridoma cells for monoclonal antibody prodn. A microtiter plate was coated with streptavidin and the histidine-biotin conjugate, and then incubated successively with a histidine-contg. specimen, a sheep anti-mouse IgG-peroxidase conjugate, and peroxidase substrate for spectrophotometric detn. of histamine.

IT **141110-92-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and immobilization of, for immunoassay)

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Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS

Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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89	RN	141110-92-1	REGISTRY

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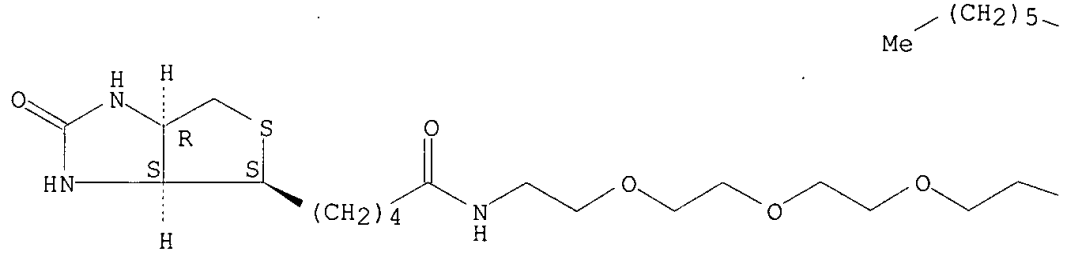
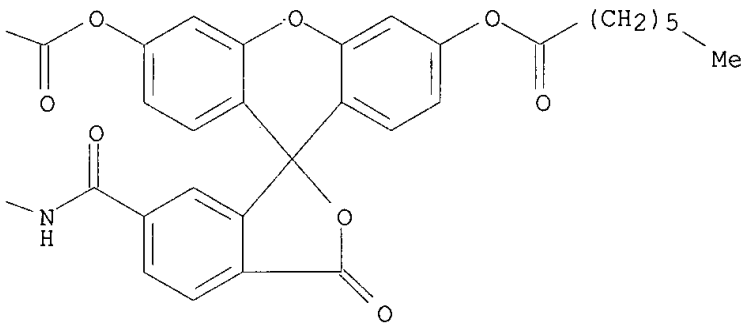
L11 ANSWER 1 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 412319-48-3 REGISTRY
CN INDEX NAME NOT YET ASSIGNED
FS STEREOSEARCH
MF C53 H68 N4 O13 S
SR CA
LC STN Files: CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



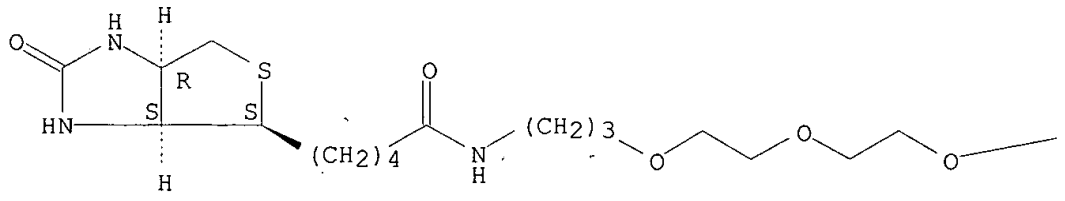
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

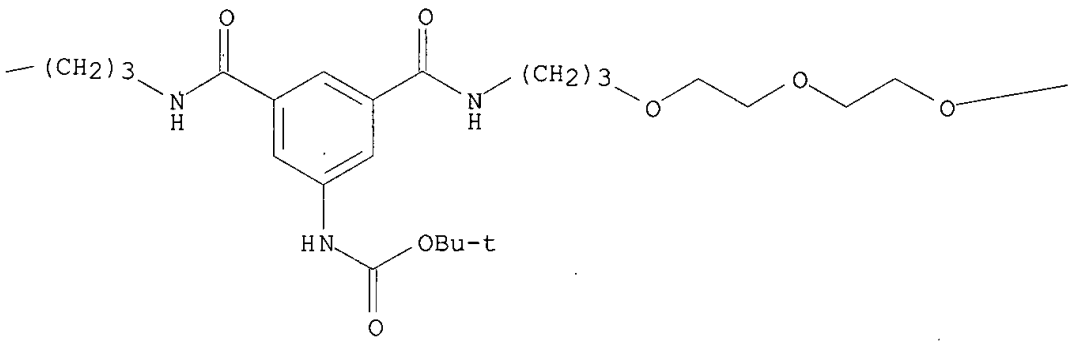
L11 ANSWER 3 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 380607-60-3 REGISTRY
CN Carbamic acid, [3-(1,17-dioxo-6,9,12-trioxa-2,16-diazaheneicos-1-yl)-5-[21-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1,17-dioxo-6,9,12-trioxa-2,16-diazaheneicos-1-yl]phenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H81 N7 O13 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

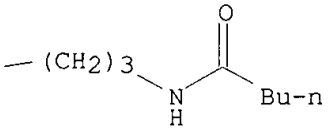
PAGE 1-A



PAGE 1-B



PAGE 1-C



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

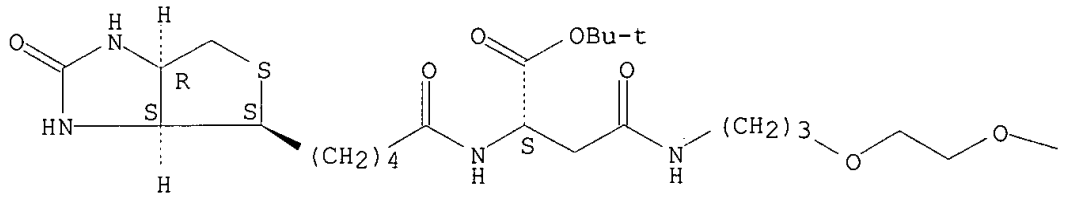
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:42919

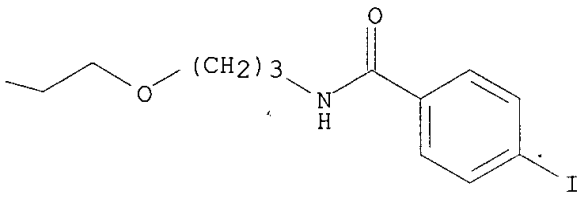
L11 ANSWER 15 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 351535-11-0 REGISTRY
CN 6,9,12-Trioxa-2,16-diazaeicosan-20-oic acid, 19-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-(4-iodophenyl)-1,17-dioxo-, 1,1-dimethylethyl ester, (19S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H54 I N5 O9 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

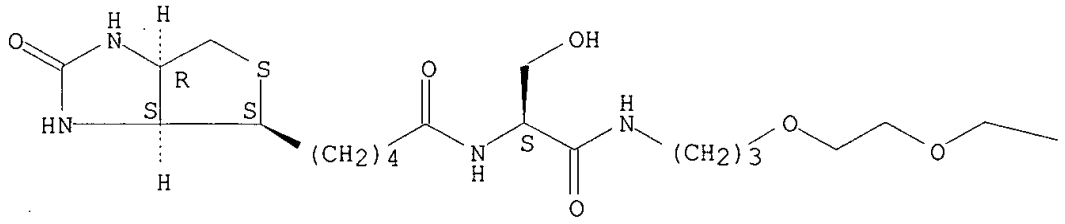
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:134197

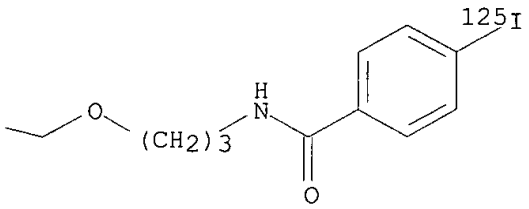
L11 ANSWER 22 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 351534-99-1 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, hexahydro-N-[(1S)-1-(hydroxymethyl)-18-[4-(iodo-125I)phenyl]-2,18-dioxo-7,10,13-trioxa-3,17-diazaoctadec-1-yl]-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H46 I N5 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



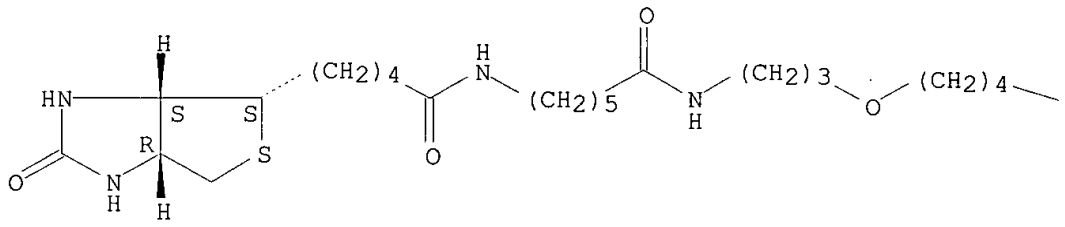
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:134197

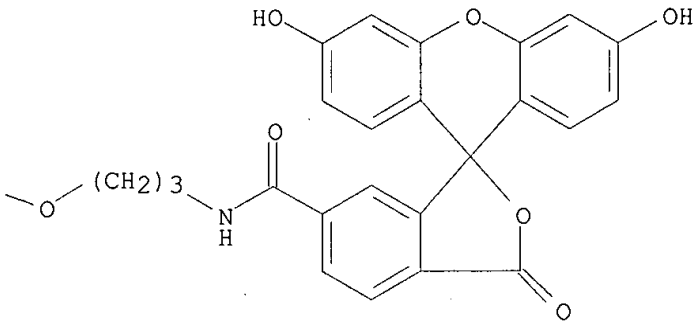
L11 ANSWER 24 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 346403-99-4 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[21-(3',6'-dihydroxy-3-oxospiro[isobenzofuran-1(3H),9'-[9H]xanthen]-6-yl)-6,21-dioxo-11,16-dioxa-7,20-diazaheneicos-1-yl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C47 H59 N5 O11 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

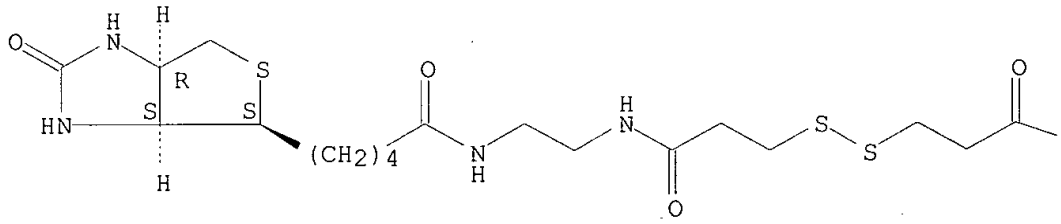
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:73673

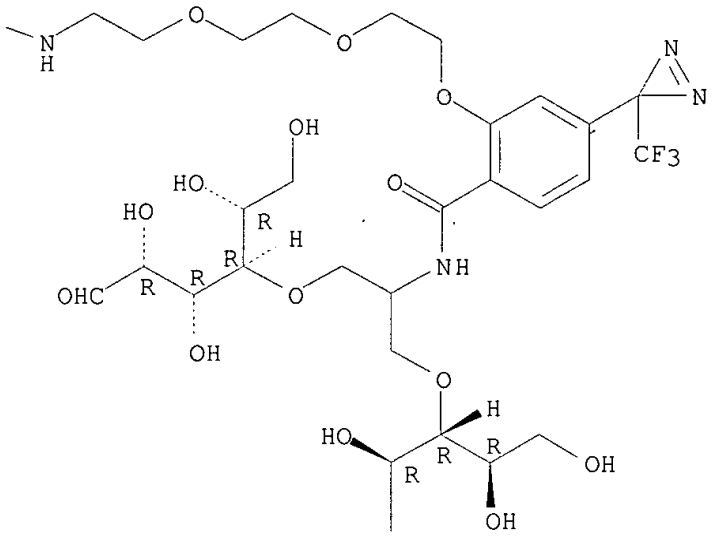
L11 ANSWER 25 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 340293-01-8 REGISTRY
CN D-Glucose, 4,4'-O-[2-[[2-[[26-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-10,17,22-trioxo-3,6-dioxa-13,14-dithia-9,18,21-triazahexacos-1-yl]oxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-1,3-propanediyl]bis- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H73 F3 N8 O20 S3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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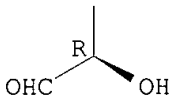


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

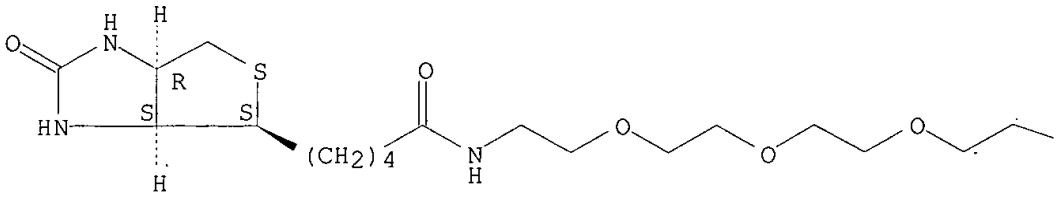
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:367106

L11 ANSWER 27 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 332941-56-7 REGISTRY
CN D-Glucose, 4-O-[(31R,32R)-63-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-31,32-dihydroxy-25,30,33,59-tetraoxo-2-[[4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-4,7,10,13,16,19,22,37,40,43,46,49,52,55-tetradecaoxa-26,29,34,58-tetraazatrihexacont-1-yl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C65 H108 F3 N9 O28 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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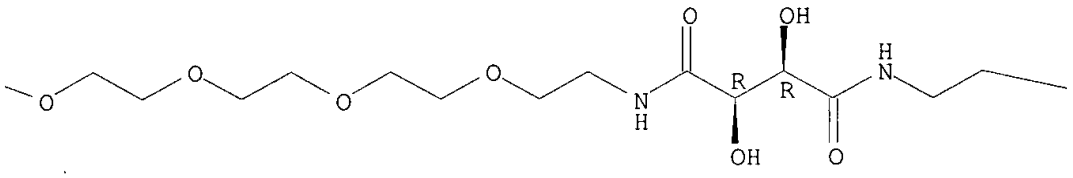
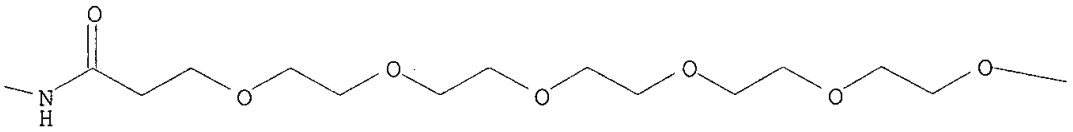
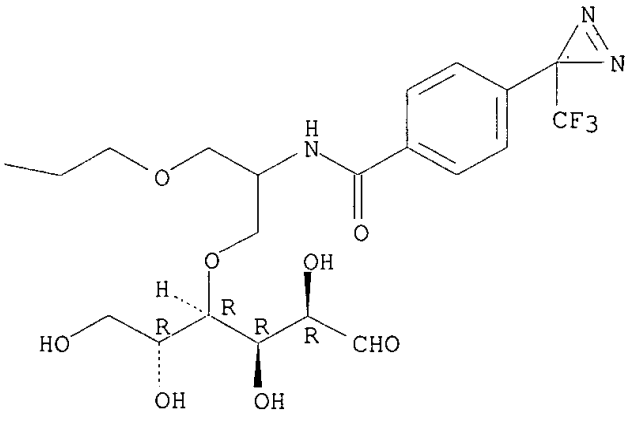


PAGE 1-C



PAGE 1-D



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

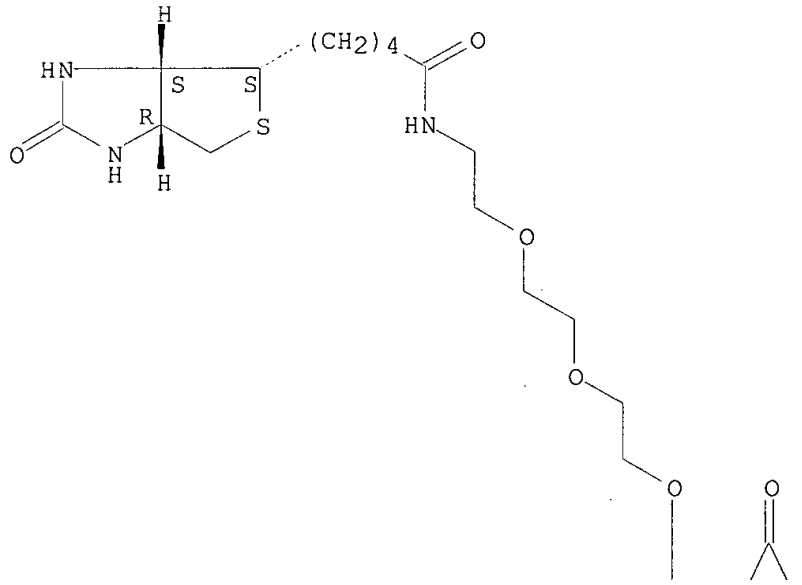
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:277052

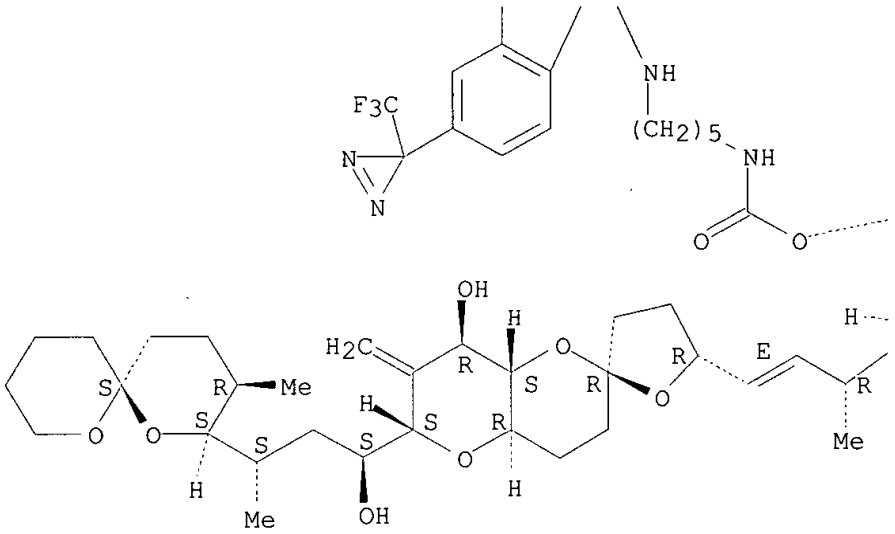
L11 ANSWER 32 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 328273-51-4 REGISTRY
CN 1,7-Dioxaspiro[5.5]undec-10-ene-2-propanoic acid, 8-[(1R,2E)-3-[(2R,4'aR,5R,6'S,8'R,8'aS)-hexahydro-8'-hydroxy-6'-[(1S,3S)-1-hydroxy-3-[(2S,3R,6S)-3-methyl-1,7-dioxaspiro[5.5]undec-2-yl]butyl]-7'-methylenespiro[furan-2(3H),2'(3'H)-pyrano[3,2-b]pyran]-5-yl]-1-methyl-2-propenyl]-5-[[[[5-[[2-[2-[2-[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethoxy]ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]pentyl]amino]carbonyl]oxy]-.alpha.-hydroxy-.alpha.,10-dimethyl-, (.alpha.R,2S,5R,6R,8S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C75 H110 F3 N7 O20 S
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.
Double bond geometry as shown.

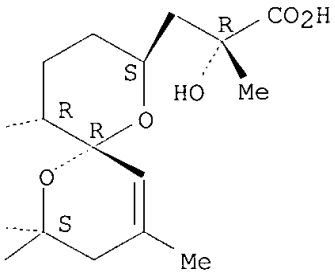
PAGE 1-A



PAGE 2-A



PAGE 2-B



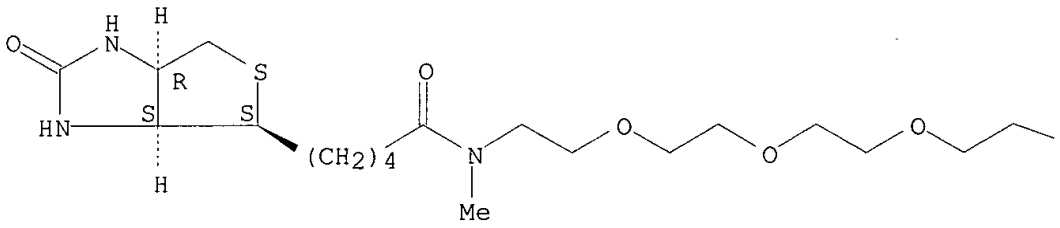
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:204239

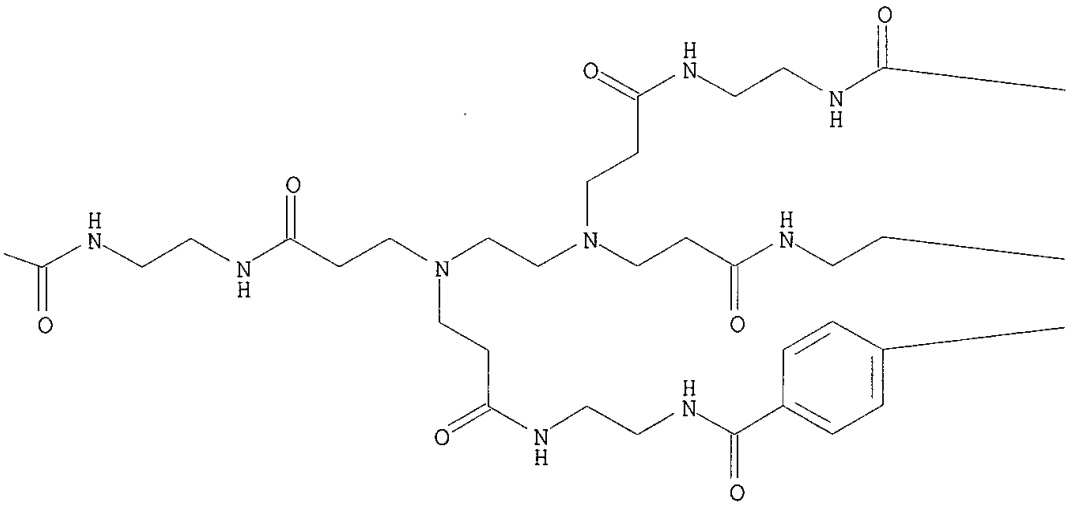
L11 ANSWER 36 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 308831-30-3 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N,N'-[20-[28-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-23-methyl-6,11,24-trioxo-3-[3-oxo-3-[[2-[[4-(tributylstannyl)benzoyl]amino]ethyl]amino]propyl]-14,17,20-trioxa-3,7,10,23-tetraazaoctacos-1-yl]-12,17,23,28-tetraoxo-3,6,9,31,34,37-hexaoxa-13,16,20,24,27-pentaazanonatriacontane-1,39-diyl]bis[hexahydro-N-methyl-2-oxo-, (3aS,3'aS,4S,4'S,6aR,6'aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C101 H177 N19 O23 S3 Sn
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

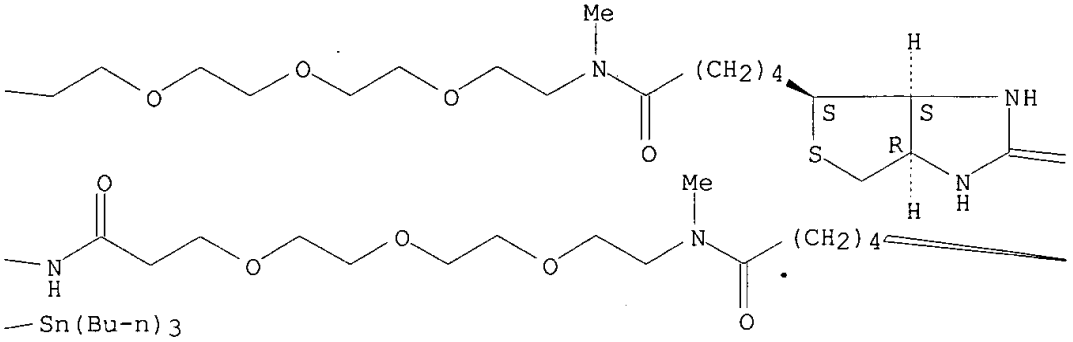
PAGE 1-A



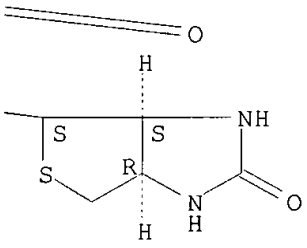
PAGE 1-B



PAGE 1-C



PAGE 1-D



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

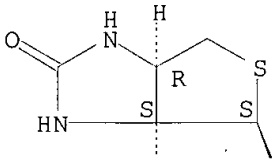
REFERENCE 1: 134:2118

L11 ANSWER 38 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 290812-04-3 REGISTRY
CN .alpha.-D-Glucopyranuronamide, O-(5R)-5-C-[3-(3-carboxy-1-oxopropyl)-1-[3-[[[2-[[[4-[(3R)-19-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-2-[[[[[2-methoxy-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]phenyl]methoxy]carbonyl]amino]methyl]-1,4,15-trioxo-2,8,11-trioxa-5,14-diazanonadec-1-yl]phenyl]thioxomethyl]amino]ethyl]amino]carbonyl]-4-nitrophenyl]-1H-1,2,4-triazol-5-yl]-.alpha.-L-arabinopyranosyl-(1.fwdarw.4)-O-2-(acetylamino)-2,6-dideoxy-.beta.-D-glucopyranosyl-(1.fwdarw.4)-O-[.beta.-D-glucopyranosyl-(1.fwdarw.6)]-O-2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl-(1.fwdarw.2)-4-C-methyl-, 3-carbamate 1-[(2R)-2-carboxy-2-[[(2Z,6E,13E)-3,8,8,14,18-pentamethyl-11-methylene-2,6,13,17-nonadecatetraenyl]oxy]ethyl hydrogen phosphate] (9CI) (CA INDEX

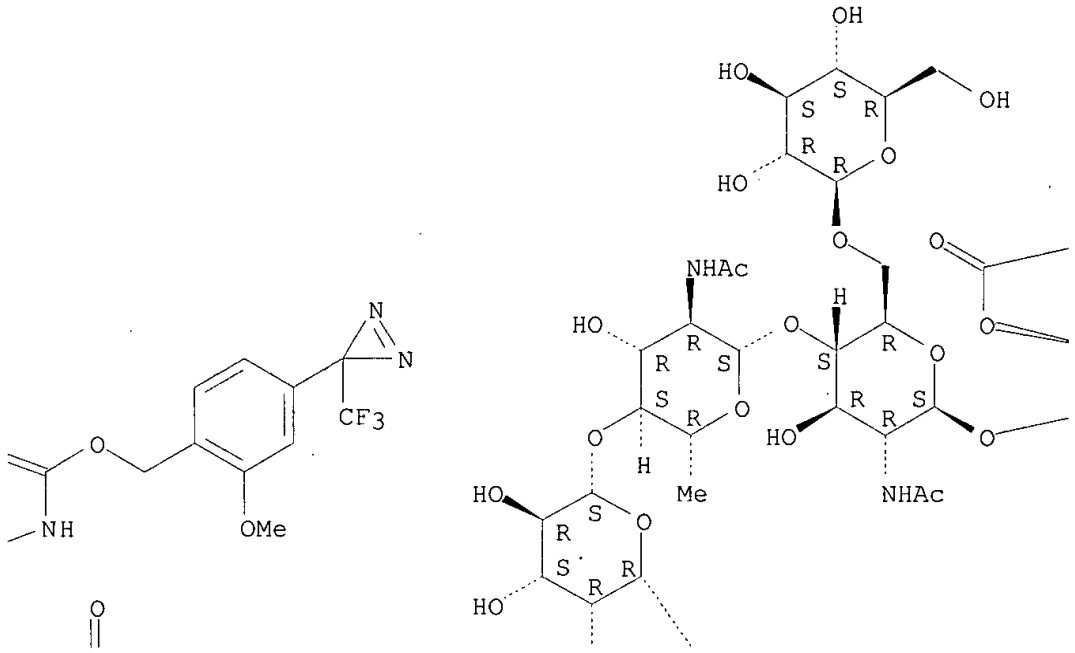
NAME)
FS STEREOSEARCH
MF C116 H161 F3 N17 O47 P S2
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.
Double bond geometry as shown.

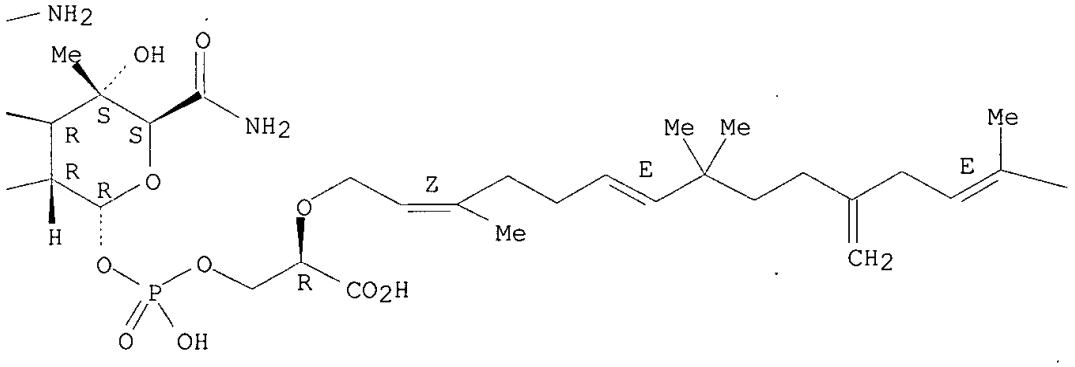
PAGE 1-A



PAGE 1-B



PAGE 1-C



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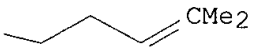

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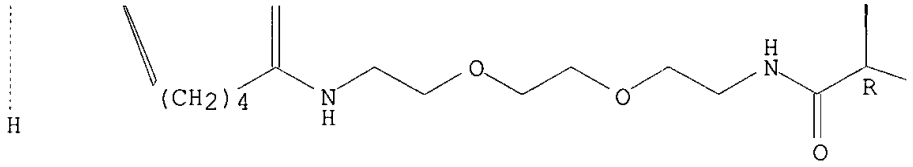
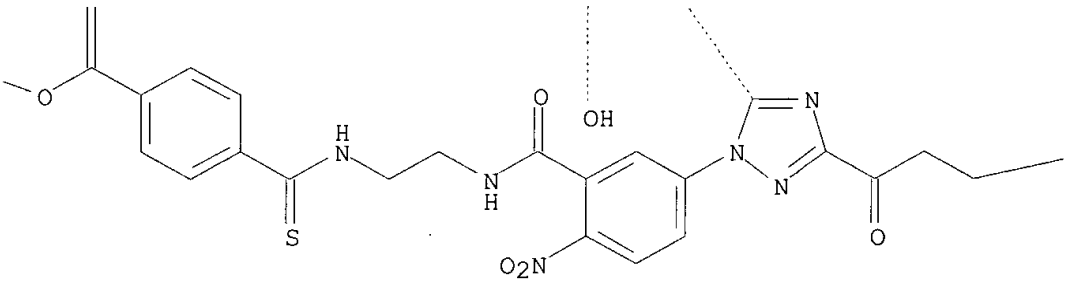


PAGE 2-B



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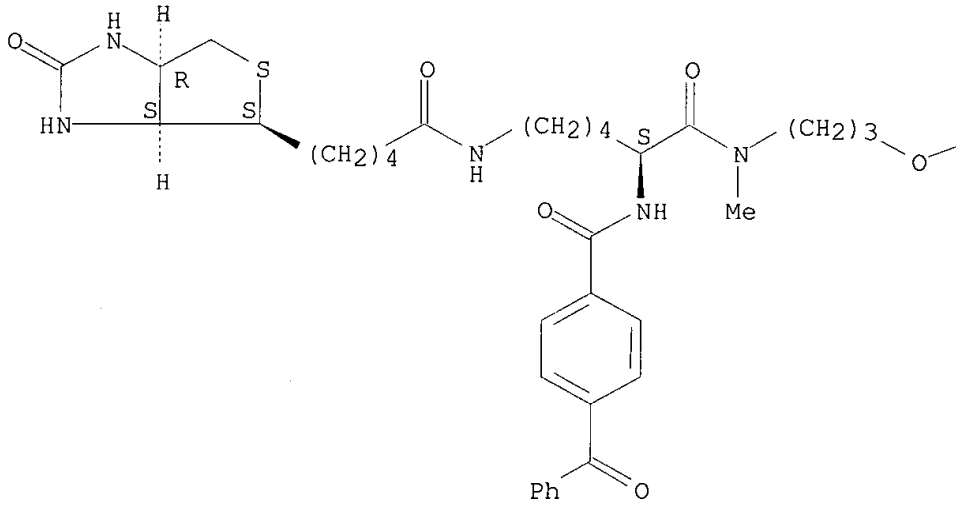
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:208058

L11 ANSWER 39 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 290330-19-7 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[(5S)-5-[(4-benzoylbenzoyl)amino]-6-[[3-[2-[[[(4-chlorophenyl)sulfonyl](2,5-difluorophenyl)amino]methyl]phenoxy]propyl]methylamino]-6-oxohexyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C53 H57 Cl F2 N6 O8 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



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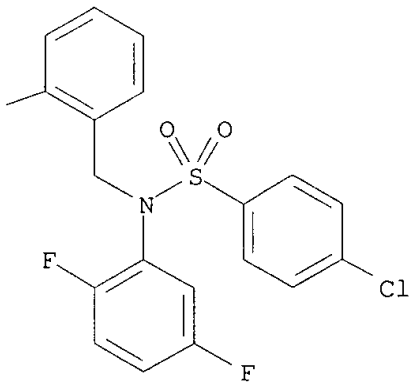


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

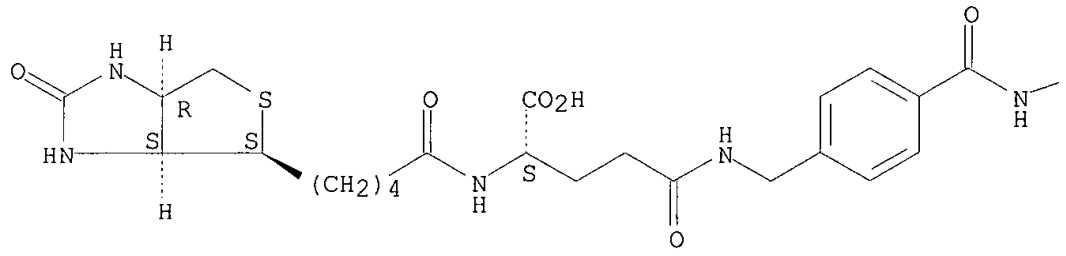
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:207678

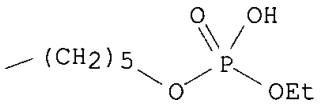
L11 ANSWER 40 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 282718-83-6 REGISTRY
CN L-Glutamine, N2-[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]-N-[[4-(9-hydroxy-9-oxido-1-oxo-8,10-dioxa-2-aza-9-phosphadodec-1-yl)phenyl]methyl]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H46 N5 O10 P S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

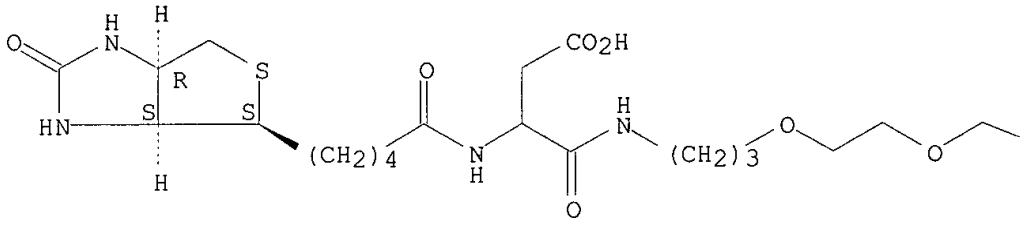
REFERENCE 1: 133:100420

L11 ANSWER 43 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 254447-31-9 REGISTRY
CN 6,9,12-Trioxa-2,16-diazaeicosan-20-oic acid, 1-[3-[[[4-[2-[bis(carboxymethyl)amino]-3-[[2-[bis(carboxymethyl)amino]cyclohexyl](carboxymethyl)amino]propyl]phenyl]amino]carbonyl]-5-isothiocyanatophenyl]-18-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1,17-dioxo- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C58 H80 N10 O20 S2

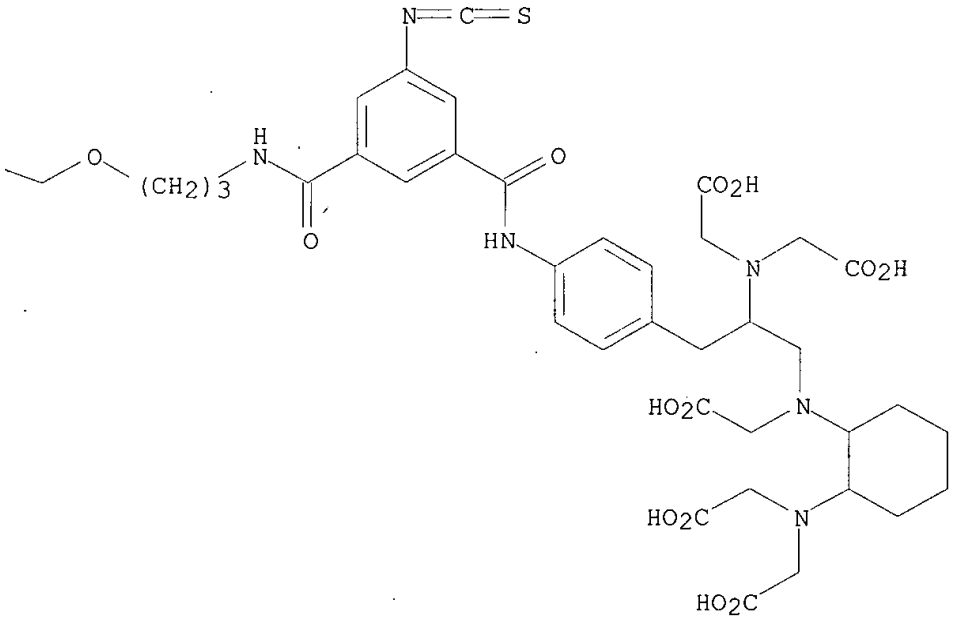
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

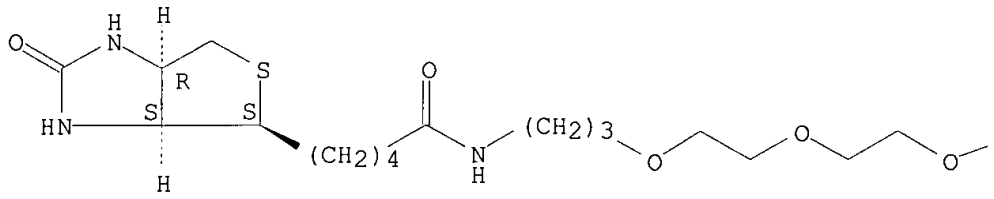
REFERENCE 1: 132:90367

L11 ANSWER 45 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 254441-28-6 REGISTRY
CN 1,3,5-Benzenetricarboxamide, N-[3-[2-[2-[3-(2,5-dihydro-2,5-dioxo-1H-pyrrol-1-yl)propoxy]ethoxy]ethoxy]propyl]-N'-[19-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-15-oxo-4,7,10-trioxa-14-azanonadec-1-

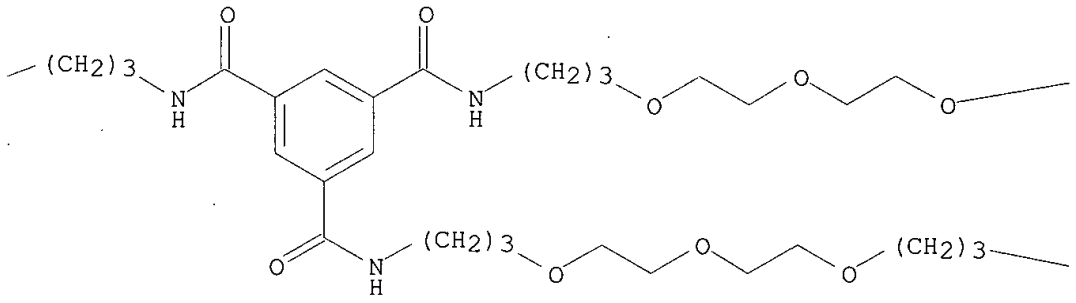
yl]-N''-[15-(4-iodophenyl)-15-oxo-4,7,10-trioxa-14-azapentadec-1-yl]-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C60 H89 I N8 O17 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

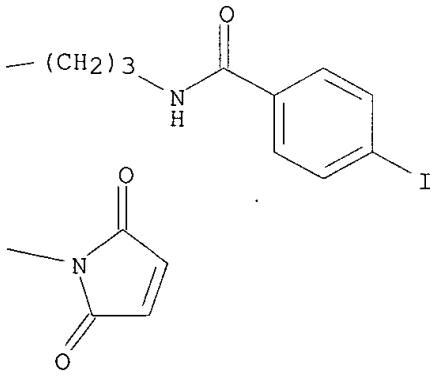
PAGE 1-A



PAGE 1-B



PAGE 1-C



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

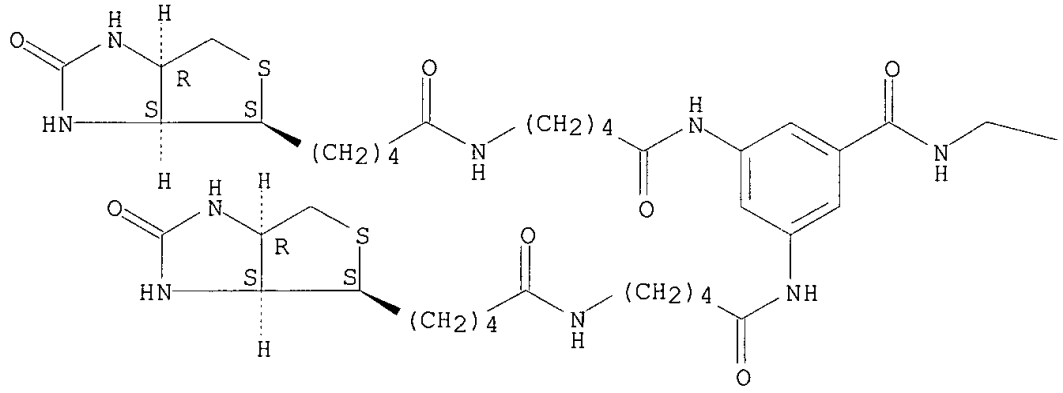
REFERENCE 1: 132:90367

REFERENCE 2: 132:90366

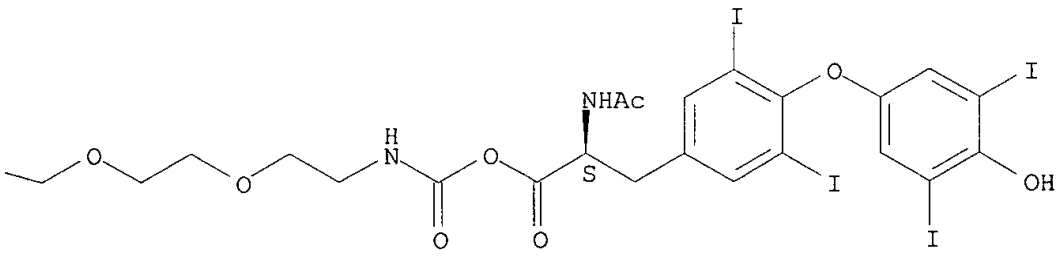
L11 ANSWER 50 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 251096-26-1 REGISTRY
CN L-Tyrosine, N-acetyl-O-(4-hydroxy-3,5-diiodophenyl)-3,5-diiodo-, anhydride with 12-[3,5-bis[[5-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxopentyl]amino]phenyl]-12-oxo-5,8-dioxa-2,11-diazadodecanoic acid (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C61 H79 I4 N11 O15 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

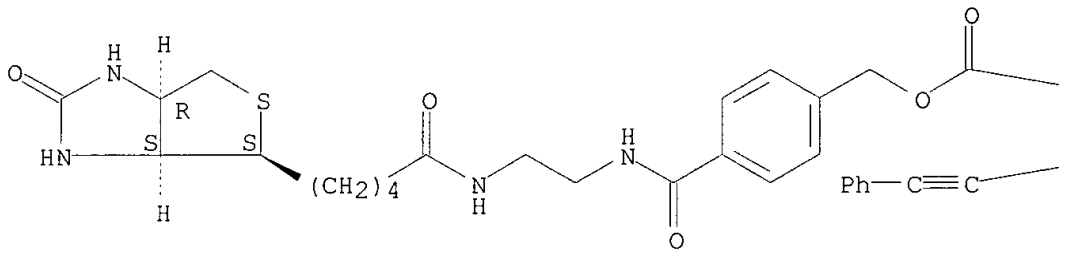
1 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:1814

L11 ANSWER 53 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 233265-81-1 REGISTRY
CN 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2-methyl-6-phenyl-4-(phenylethynyl)-, 5-ethyl 3-[[4-[[[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethyl]amino]carbonyl]phenyl]methyl] ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C44 H47 N5 O7 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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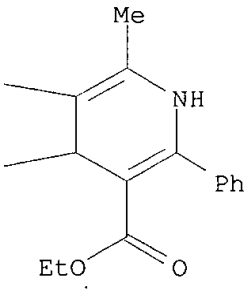


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

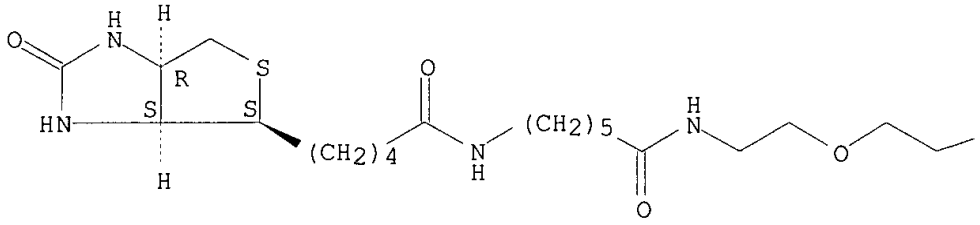
REFERENCE 1: 131:110893

L11 ANSWER 54 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 207971-25-3 REGISTRY
CN D-Mannose, 4,4'-O-[2-[[2-[[21-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-10,17-dioxo-3,6-dioxa-9,16-diazaheneicos-1-yl]oxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-1,3-propanediyl]bis-

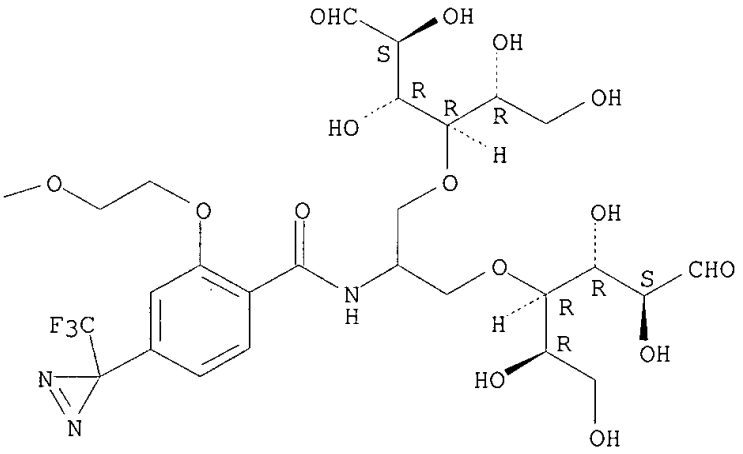
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C46 H70 F3 N7 O19 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

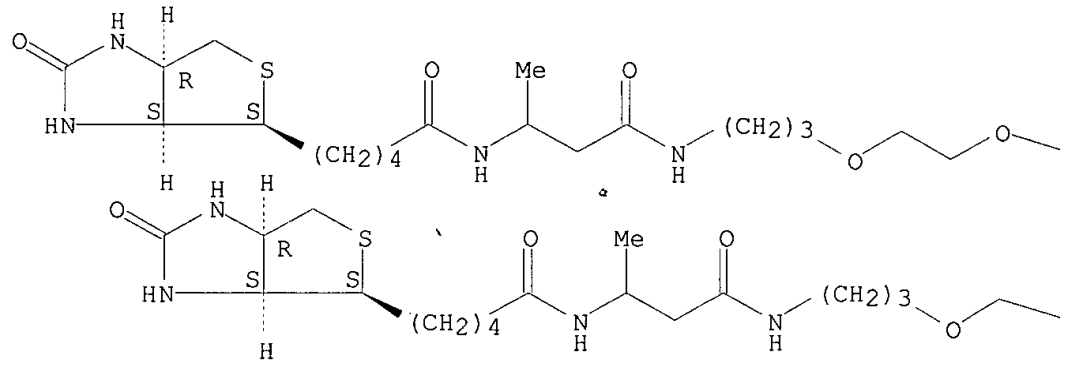
REFERENCE 1: 129:25290

L11 ANSWER 56 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 195370-62-8 REGISTRY
CN 1,3,5-Benzenetricarboxamide, N,N',N''-tris[23-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-17-methyl-15,19-dioxo-4,7,10-trioxa-14,18-diazatricos-1-yl]-, [3aS-[3a.alpha.,4.beta.(3aR*,4R*,6aS*),4(3aR*,4R*,6aS*),6a.alpha.]]-[partial]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH

MF C81 H135 N15 O21 S3
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



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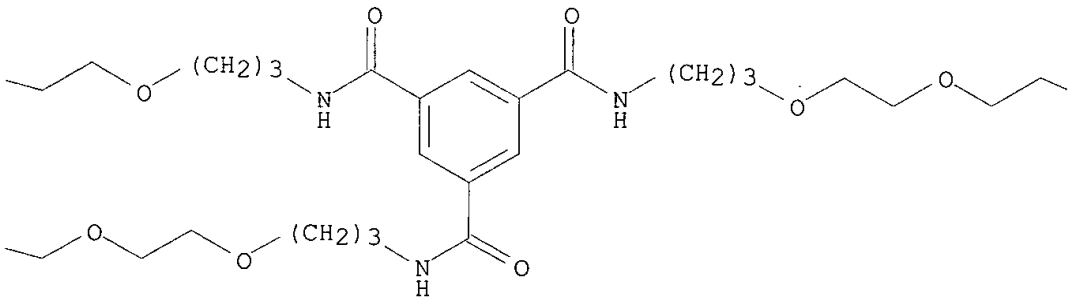
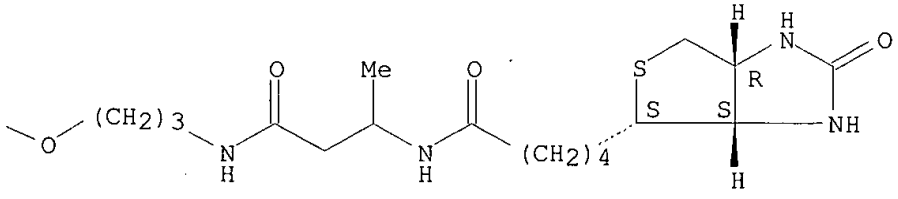


PAGE 1-C



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

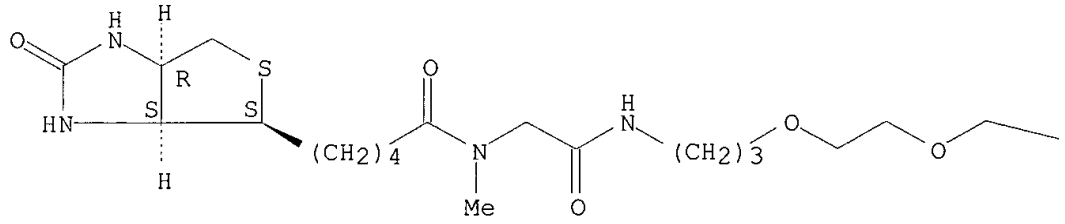
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:298612

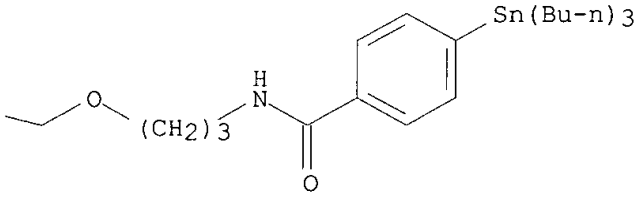
L11 ANSWER 57 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 194920-71-3 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2,18-dioxo-18-[4-(tributylstannyl)phenyl]-7,10,13-trioxa-3,17-diazaoctadec-1-yl]hexahydro-N-methyl-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2,18-dioxo-18-[4-(tributylstannyl)phenyl]-7,10,13-trioxa-3,17-diazaoctadec-1-yl]hexahydro-N-methyl-2-oxo-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]-
FS STEREOSEARCH
MF C42 H73 N5 O7 S Sn
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

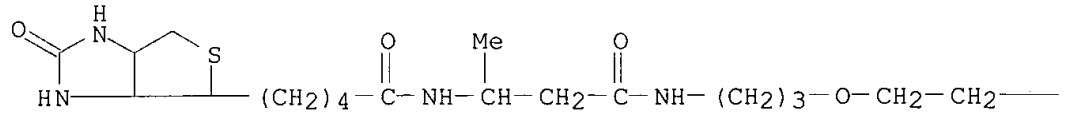
REFERENCE 1: 135:134197

REFERENCE 2: 127:220519

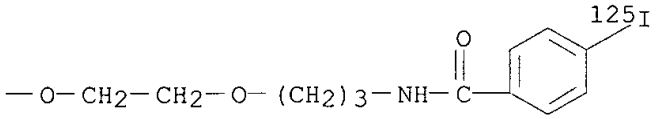
L11 ANSWER 65 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 192721-01-0 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, hexahydro-N-[19-[4-(iodo-125I)phenyl]-1-methyl-3,19-dioxo-8,11,14-trioxa-4,18-diazanonadec-1-yl]-2-oxo- (9CI) (CA INDEX NAME)

FS 3D CONCORD
MF C31 H48 I N5 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 1-B

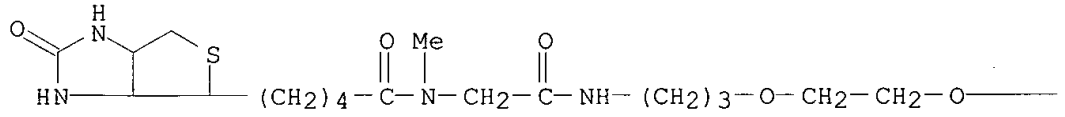


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

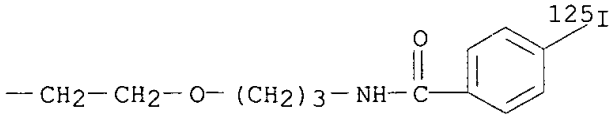
REFERENCE 1: 127:121587

L11 ANSWER 66 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 192720-99-3 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, hexahydro-N-[18-[4-(iodo-125I)phenyl]-2,18-dioxo-7,10,13-trioxa-3,17-diazaoctadec-1-yl]-N-methyl-2-oxo- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C30 H46 I N5 O7 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 1-B

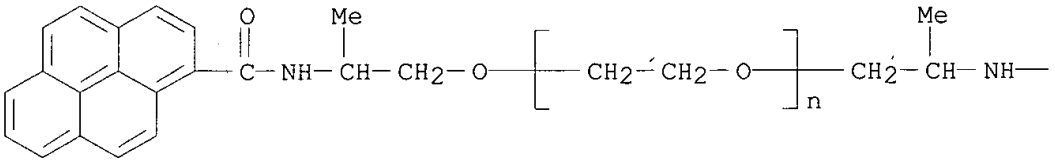


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:121587

L11 ANSWER 77 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 192432-86-3 REGISTRY
CN Poly(oxy-1,2-ethanediyl), .alpha.-[2-[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]propyl]-.omega.-[2-[(1-pyrenylcarbonyl)amino]propoxy]-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)
MF (C2 H4 O)n C33 H38 N4 O4 S
CI PMS
PCT Polyether
SR CA
LC STN Files: CA, CAPLUS

PAGE 1-A



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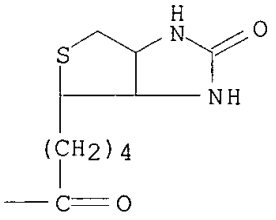

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 127:106189

L11 ANSWER 81 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 189887-17-0 REGISTRY
CN Cobinamide, Ne,Ne'-[[5-[[6-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]-1-oxohexyl]amino]-1,3-phenylene]bis(15-oxo-4,7,10-trioxa-14-azapentadecane-15,1-diyl)]bis[Co-(cyano-.kappa.C)-, bis(dihydrogen phosphate) (ester), bis(inner salt), P.fwdarw.3':P'.fwdarw.3'''-diester with (5,6-dimethyl-1-.alpha.-D-ribofuranosyl-1H-benzimidazole-.kappa.N3) (9CI) (CA INDEX NAME)
MF C170 H246 Co2 N34 O39 P2 S
CI CCS
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:38641

REFERENCE 2: 126:343813

L11 ANSWER 83 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 186263-07-0 REGISTRY
CN Butanediamide, N4-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-2-[[2-[2-[2-[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethoxy]ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-, (2S)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Butanediamide, N4-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-2-[[2-[2-[2-[2-[[5-[(3aS,4S,6aR)-hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl]-1-oxopentyl]amino]ethoxy]ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-, (S)-
OTHER NAMES:
CN BDGA
FS STEREOSEARCH
MF C37 H52 F3 N9 O13 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

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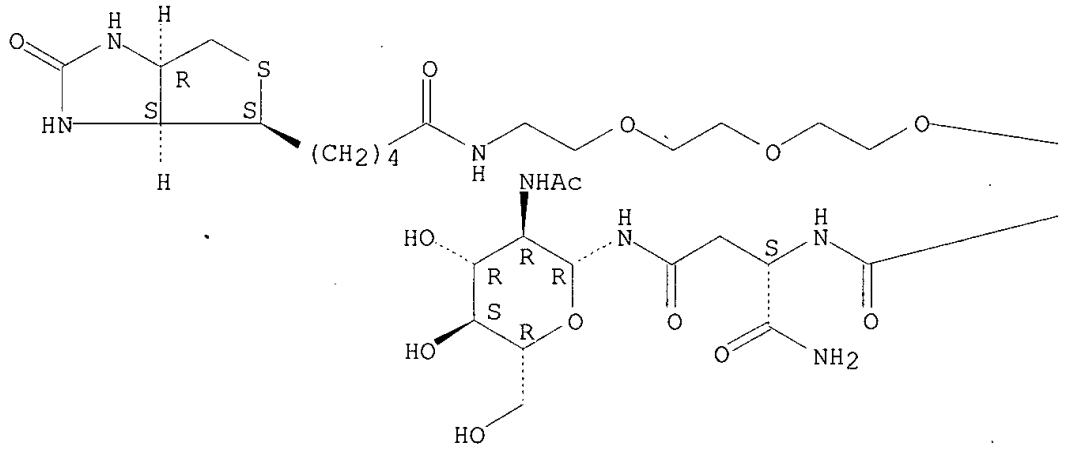

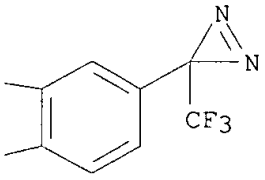

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:119561

REFERENCE 2: 128:72612

REFERENCE 3: 126:289755

REFERENCE 4: 126:114867

L11 ANSWER 84 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 175663-44-2 REGISTRY
CN L-Asparagine, N-[2-(acetylamino)-2-deoxy-.beta.-D-glucopyranosyl]-N2-[2-[2-[2-[2-[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]ethoxy]ethoxy]ethoxy]-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H51 F3 N8 O14 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

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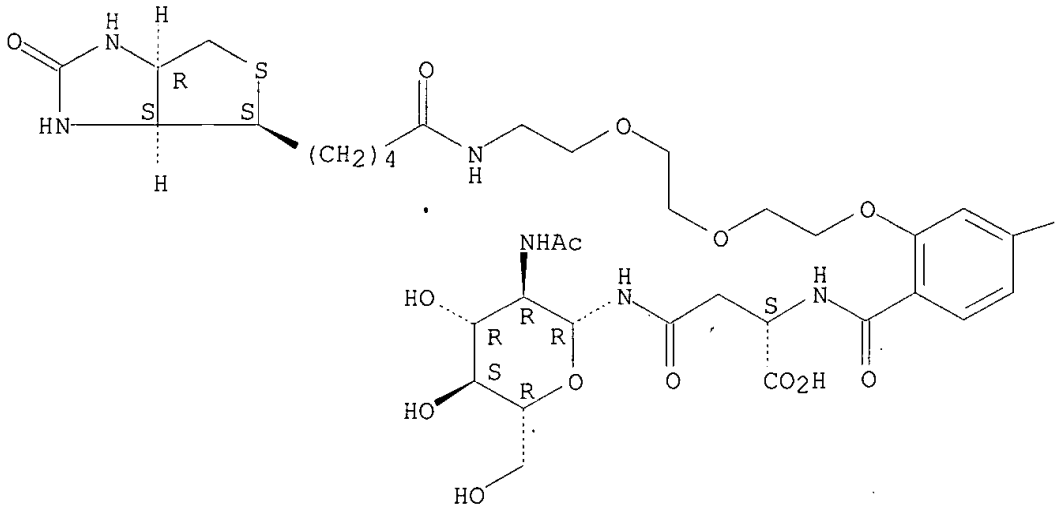

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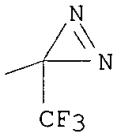


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

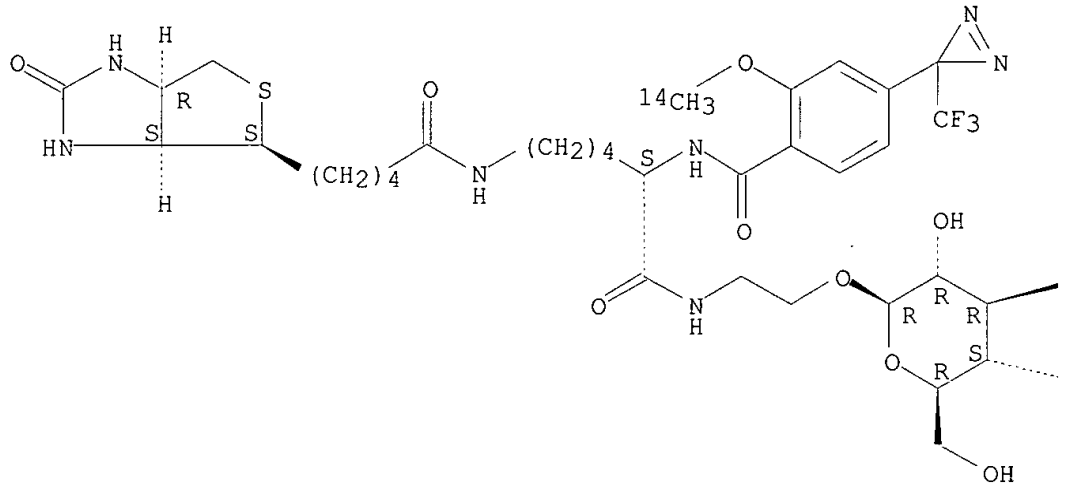
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 124:283427

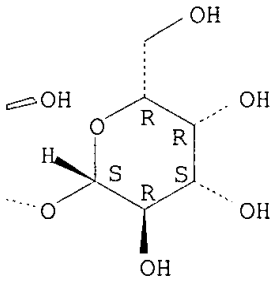
L11 ANSWER 85 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 173949-63-8 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[6-[[2-[(4-O-.beta.-D-galactopyranosyl-.beta.-D-glucopyranosyl)oxy]ethyl]amino]-5-[[2-(methoxy-14C)-4-[3-(trifluoromethyl)-3H-diazirin-3-yl]benzoyl]amino]-6-oxohexyl]hexahydro-2-oxo-, [3aS-[3a.alpha.,4.beta.(R*),6a.alpha.]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H58 F3 N7 O16 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

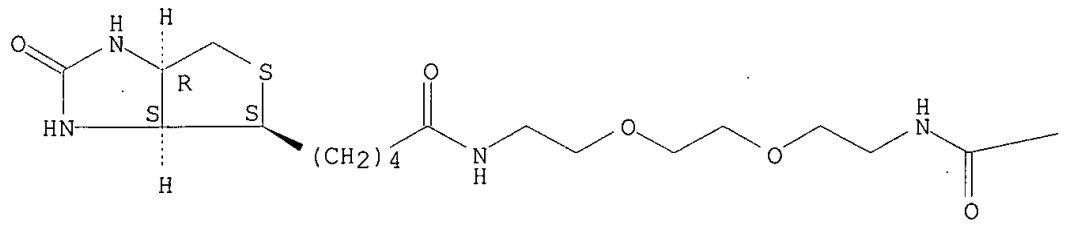
REFERENCE 1: 124:176693

L11 ANSWER 87 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 168411-59-4 REGISTRY
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[2-[2-[2-[(4-azidobenzoyl)amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H33 N7 O5 S

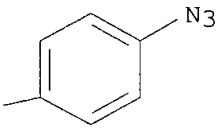
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

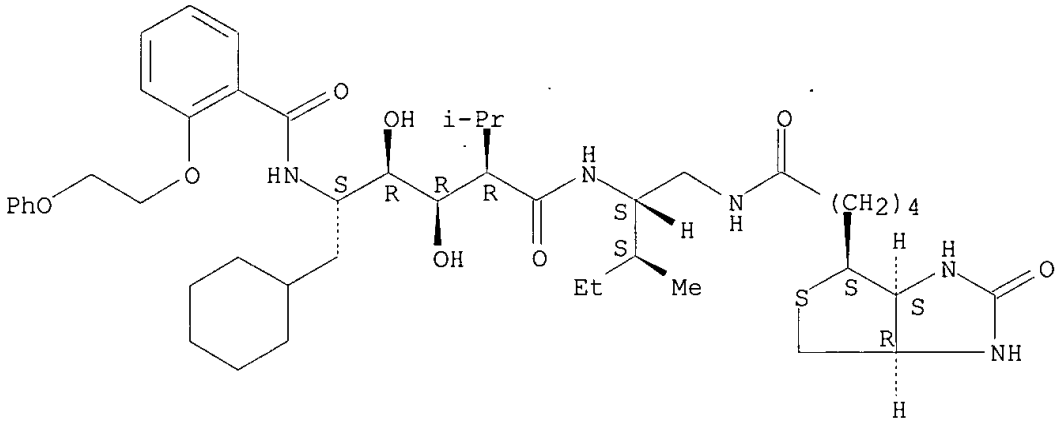


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:222328

L11 ANSWER 88 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 153805-31-3 REGISTRY
CN L-Idonamide, 6-cyclohexyl-2,5,6-trideoxy-N-[1-[[[5-(hexahydro-2-oxo-1H-thieno[3,4-d]imidazol-4-yl)-1-oxopentyl]amino]methyl]-2-methylbutyl]-2-(1-methylethyl)-5-[[2-(2-phenoxyethoxy)benzoyl]amino]-, [3aS-[3a.alpha.,4.beta.(1R*,2R*),6a.alpha.]]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1H-Thieno[3,4-d]imidazole, L-idonamide deriv.
FS STEREOSEARCH
MF C46 H69 N5 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



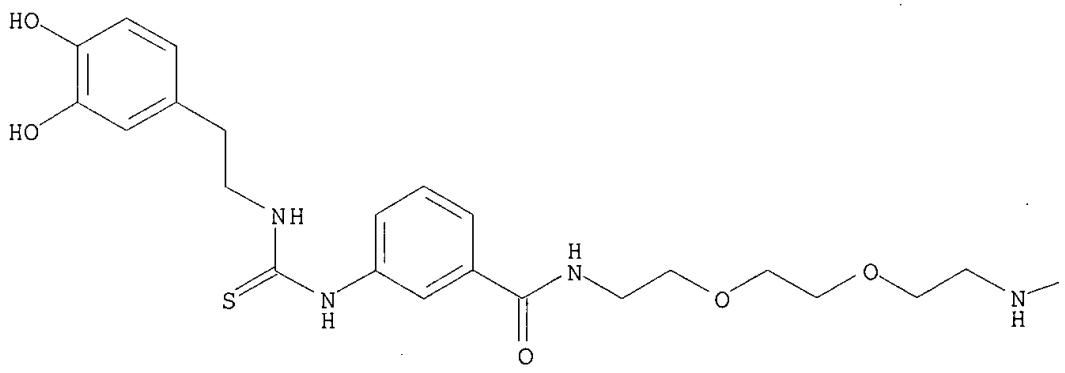
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

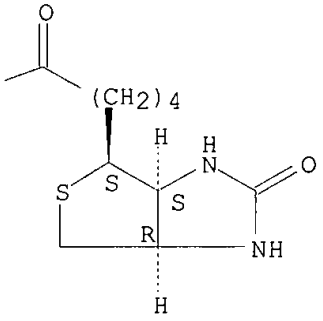
REFERENCE 1: 120:245753

L11 ANSWER 89 OF 89 REGISTRY COPYRIGHT 2002 ACS
RN 141110-92-1 REGISTRY
CN 1H-Thieno[3,4-b]imidazole-4-pentanamide, N-[2-[2-[2-[[3-[[[[2-(3,4-dihydroxyphenyl)ethyl]amino]thioxomethyl]amino]benzoyl]amino]ethoxy]ethoxy]ethyl]hexahydro-2-oxo-, [3aS-(3a.alpha.,4.beta.,6a.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C32 H44 N6 O7 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

PAGE 1-A





PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:210738

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FILE 'HCAPLUS' ENTERED AT 19:45:31 ON 10 MAY 2002
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FILE COVERS 1907 - 10 May 2002  VOL 136 ISS 19
FILE LAST UPDATED: 8 May 2002  (20020508/ED)

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information on CAS roles, enter HELP ROLES at an arrow prompt or use
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=> d stat que
L18             8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (DIFFERENTIAL(W)LABEL?)(L)SPEC
                  TROMET?


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L18  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:276137  HCAPLUS
DOCUMENT NUMBER:          136:305090
TITLE:                    Whole cell engineering by mutagenizing a substantial
                          portion of a starting genome and combining mutations
                          with optional reiteration, identifying protein
                          profiles by differential labeling
                          and mass spectrometry, and by metabolic flux
                          analysis
INVENTOR(S):              Short, Jay M.; Fu, Pengcheng; Latterich, Martin; Wei,
                          Jing; Levin, Michael
PATENT ASSIGNEE(S):       Diversa Corporation, USA
SOURCE:                   PCT Int. Appl., 869 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ----------------  ----  --------       ---------------  --------
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WO 2002029032 A2 20020411 WO 2001-US31004 20011001
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2001096551 A2 20011220 WO 2001-US19367 20010614
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-677584 A2 20000930
US 2001-279702P P 20010328
WO 2001-US19367 W 20010614
US 2000-594459 A2 20000614

AB An invention comprising cellular transformation, directed evolution, and screening methods for creating novel transgenic organisms having desirable properties. In one embodiment, this invention provides a method of generating a transgenic organism, such as a microbe or a plant, having a plurality of traits that are differentially activatable. This invention also provides a method of retooling genes and gene pathways by the introduction of regulatory sequences, such as promoters, that are operable in an intended host, this conferring operability to a novel gene pathway when it is introduced into an intended host. For example a novel man-made gene pathway, generated based on microbially-derived progenitor templates, that is operable in a plant cell. This invention also provides a method of generating novel host organisms having increased expression of desirable traits, recombinant genes, and gene products. This invention provides novel methods for detg. polypeptide profiles, and protein expression variations, which methods are applicable to all sample types disclosed herein. The present invention provides methods of simultaneously identifying and quantifying individual proteins in complex protein mixts. by fragmentation, **differential labeling**, and tandem mass **spectrometry**. Addnl. this invention provides methods for cellular and metabolic engineering of new and modified phenotypes by using "online" or "real-time" metabolic flux anal.

L18 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:154547 HCAPLUS
TITLE: Quantitative proteomics strategy involving the selection of peptides containing both cysteine and histidine from tryptic digests of cell lysates
AUTHOR(S): Wang, Shihong; Zhang, Xiang; Regnier, Fred E.
CORPORATE SOURCE: Department of Chemistry, Purdue University, West Lafayette, IN, 47907-1393, USA
SOURCE: Journal of Chromatography, A (2002), 949(1-2), 153-162
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper describes a procedure for quant. proteomics that selects

peptides contg. both cysteine and histidine residues from tryptic digests of cell lysates. Cysteine-contg. peptides were selected first by covalent chromatog. using thiol disulfide exchange. Following the release of cysteine-contg. peptides from the covalent chromatog. column with reductive cleavage, histidine-contg. peptides were captured by passage through an immobilized metal affinity chromatog. column loaded with copper. Quantification was achieved in a four-step process involving (i) **differential labeling** of control and exptl. samples with isotopically differing forms of succinic anhydride, (ii) mixing the two globally labeled samples, (iii) fractionating the labeled peptides by reversed-phase liq. chromatog., and (iv) detg. the isotope ratio in individual peptides by mass **spectrometry**. The results of these studies indicate that by selecting peptides contg. both cysteine and histidine, the complexity of protein digests could be substantially reduced. Up-regulated proteins from plasmid bearing Escherichia coli that had been induced with iso-Pr .beta.-thiogalacto-pyranoside were identified and quantified by the global internal std. technol. (GIST) described above. Database searches were greatly simplified because the no. of possible peptide candidates was reduced more than 95%.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:688465 HCAPLUS
DOCUMENT NUMBER: 132:75555
TITLE: Mass Spectrometry to Characterize the Binding of a Peptide to a Lipid Surface
AUTHOR(S): MacPhee, Cait E.; Howlett, Geoffrey J.; Sawyer, William H.
CORPORATE SOURCE: Russell Grimwade School of Biochemistry and Molecular Biology, University of Melbourne, Parkville, 3052, Australia
SOURCE: Analytical Biochemistry (1999), 275(1), 22-29
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The binding of an amphipathic .alpha.-helical peptide to small unilamellar lipid vesicles has been examd. using chem. derivitization and mass **spectrometry**. The peptide is derived from the sequence of human apolipoprotein C-II (apoC-II), the protein activator of lipoprotein lipase (LpL). ApoC-II19-39 forms approx. 60% .alpha.-helix upon binding to model egg yolk phosphatidylcholine small unilamellar vesicles. Measurement of the affinity of the peptide for lipid by spectrophotometric methods is complicated by the contribution of scattered light to optical signals. Instead, we characterize the binding event using the **differential labeling** of lysine residues by the lipid- and aq.-phase cross-linkers, disuccinimidyl suberate (DSS) and bis(sulfosuccinimidyl) suberate (BS3), resp. In aq. soln., the three lysine residues of the peptide are accessible to both cross-linkers. In the presence of lipid, the C-terminal lysine residue becomes inaccessible to the lipid-phase cross-linker DSS, but remains accessible to the aq.-phase cross-linker, BS3. We use mass **spectrometry** to characterize this binding event and to derive a dissocn. const. for the interaction (Kd = 5 .mu.M). We also provide evidence for the formation of dimeric cross-linked peptide when high densities of peptide are bound to the lipid surface. (c) 1999 Academic Press.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:367273 HCAPLUS
DOCUMENT NUMBER: 125:80988
TITLE: Advances in high resolution SIMS studies of BrdU-labeled human metaphase chromosomes
AUTHOR(S): Levi-Setti, R.; Chabala, J. M.; Gavrilov, K.; Espinosa, R., III; Le Beau, M. M.
CORPORATE SOURCE: Dep. Physics, Univ. Chicago, Chicago, IL, 60637, USA
SOURCE: Cell. Mol. Biol. (Paris) (1996), 42(3), 301-324
CODEN: CMOBEF; ISSN: 0145-5680
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The detection of bromine in human metaphase chromosomes labeled with the thymidine-analog bromodeoxyuridine (BrdU), by imaging secondary ion mass **spectrometry** (SIMS) with a high resoln. scanning ion microprobe, provides detailed maps of the AT distribution within the chromosomes. Similarly, maps of the emitted CN-mol. ions describe the overall DNA, RNA and protein distribution, details of which are also revealed by maps of the divalent cations Ca2+ and Mg2+. Base-specific banding patterns (SIMS bands), mimicking the well known G- or Q-bands resulting from conventional staining methods for optical microscopy, are obsd. in several prepns., more noticeably in mitotic cells at the 1st cell division, after in situ DNA denaturation or Giemsa staining. A structured distribution, seemingly related to G/Q-banding patterns, is also obsd. in the Mg2+ and Ca2+ maps. The **differential label** signal intensities between sister chromatids, at the 2nd cell division and beyond, manifest the occurrence of sister chromatid exchanges (SCE), occurring both spontaneously and induced following exposure of the cells to the chem. aphidicolin (an inhibitor of DNA replication). Imaging SIMS emerges as a powerful investigative method for the study of chromosome structure and the elucidation of banding mechanisms, to assess the removal of proteins and DNA involved in chromosome prepn. in in situ procedures, and in the study of a no. of cytogenetic phenomena.

L18 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:273444 HCAPLUS
DOCUMENT NUMBER: 122:75018
TITLE: Identification of posttranslationally modified 18-kilodalton protein from rice as eukaryotic translation initiation factor 5A
AUTHOR(S): Mehta, Arkesh M.; Saftner, Robert A.; Mehta, Roshni A.; Davies, Peter J.
CORPORATE SOURCE: Section Plant Biol., Cornell Univ., Ithaca, NY, 14853-5908, USA
SOURCE: Plant Physiol. (1994), 106(4), 1413-19
CODEN: PLPHAY; ISSN: 0032-0889
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Using anther-derived rice (Oryza sativa L.) cell-suspension cultures, we have identified an 18-kD protein that is posttranslationally modified by spermidine and is influenced by endogenous polyamine levels. The posttranslationally modified residue has been identified as the unusual amino acid hypusine [N.epsilon.-(4-amino-2-hydroxybutyl)lysine] by reverse-phase high-performance liq. chromatog. and gas chromatog.-mass-**spectrometry** analyses. **Differential labeling** of the protein with labeled amines provided evidence that the butylamine moiety of spermidine is the immediate precursor of the hypusine residue in the protein. The eukaryotic translation initiation factor 5A (eIF-5A) is

the only known mammalian protein that undergoes a similar posttranslational modification with hypusine. The purified 18-kD protein co-electrophoreses with human translational initiation factor eIF-5A in both isoelec. focusing and sodium dodecyl sulfate-polyacrylamide gels. The purified protein from rice stimulated methionyl-puromycin synthesis in vitro, indicating its functional similarity to mammalian eIF-5A. The results presented provide evidence that the posttranslationally modified 18-kD protein from rice contg. hypusine is eIF-5A and suggest the conservation of hypusine-contg. translation initiation factor eIF-5A in eukaryotes.

L18 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:466320 HCAPLUS
DOCUMENT NUMBER: 119:66320
TITLE: Identification of sites for feedback regulation of glutamine 5-phosphoribosylpyrophosphate amidotransferase by nucleotides and relationship to residues important for catalysis
AUTHOR(S): Zhou, Gaochao; Charbonneau, Harry; Colman, Roberta F.; Zalkin, Howard
CORPORATE SOURCE: Dep. Biochem., Purdue Univ., West Lafayette, IN, 47907-1153, USA
SOURCE: J. Biol. Chem. (1993), 268(14), 10471-81
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Glutamine phosphoribosylpyrophosphate amidotransferase, the key regulatory enzyme for de novo purine nucleotide synthesis, is subject to feedback regulation by adenine and guanine nucleotides. Affinity labeling with 5'-p-fluorosulfonylbenzoyladenosine (FSBA) and 8-azidoadenosine 5'-monophosphate (N3-AMP) was used to identify purine nucleotide sites for feedback control of the Escherichia coli amidotransferase. FSBA inactivated the amidotransferase with satn. kinetics. Specificity for inactivation was shown by the covalent attachment of 2.0-2.4 equiv of [3H] sulfobenzoyladenosine (SBA) per subunit and protection by GMP and AMP against inactivation and incorporation of [3H}SBA. Six chymotryptic peptides modified with [3H]SBA were isolated and identified by **differential labeling** followed by high performance liq. chromatog. and radioactivity. Mass **spectrometry** and Edman degrdn. anal. were used to identify 5 residues that were covalently modified by [3H]SBA: Tyr74, Tyr258, Lys326, Tyr329, and Tyr465. Tyr258 was also modified ny N3-AMP. Mutant enzymes K326Q and Y329A had activity similar to that of the wild type enzyme. However, both mutants exhibited decreased sensitivity to inhibition by GMP and decreased binding of GMP but were inhibited by AMP. Mutant enzymes Y74A and Y258F were normally feedback-inhibited but were defective in glutamine amide transfer and synthase functions, resp. Therefore Tyr74 and Tyr258 are important for activity and modification by FSBA and N3-AMP accounts for enzyme inactivation. These results localize residues important for catalysis in close proximity to a site for nucleotide binding. Two addnl. mutant enzymes, G331I and N351A, were constructed which were refractory to inhibition by GMP with little change in inhibition by AMP. A replacement of Tyr465 indicates that this residue is not essential for catalysis or feedback inhibition. Overall, these results are interpreted in terms of a two-nucleotide site model with Lys326, Tyr329, Gly331, and Asn351 defining a site required for inhibition by GMP. A second nucleotide site not affinity labeled by analogs is very close to or overlaps with the catalytic site.

L18 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:631520 HCAPLUS
DOCUMENT NUMBER: 117:231520
TITLE: Site-specific glycation of lens crystallins by ascorbic acid
AUTHOR(S): Ortwerth, Beryl J.; Slight, Simon H.; Prabhakaram, Malladi; Sun, Yiping; Smith, Jean B.
CORPORATE SOURCE: Mason Inst. Ophthalmol., Univ. Missouri, Columbia, MO, USA
SOURCE: Biochim. Biophys. Acta (1992), 1117(2), 207-15
CODEN: BBACAQ; ISSN: 0006-3002
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The oxidn. of ascorbic acid leads to the formation of several compds. which are capable of reacting with protein amino groups via a Maillard reaction. Radioactivity from [1-14C]ascorbic acid was linearly incorporated into lens crystallins over a 10 day period in the presence of NaCNBH3. This rate of incorporation was 6-7-fold more rapid than that obtained with [14C]glucose under the same conditions. SDS-PAGE showed a linear incorporation into all the crystallin subunits. [1-14C]ascrobic acid-labeled .alpha.-crystallin was sepd. into its component A and B subunits, and each was digested with chymotrypsin. HPLC peptide anal. showed a **differential labeling** of the various lysine residues. Anal. of the peptides by mass **spectrometry** allowed the identification of the sites and the extent of modification. These values ranged from 6% for Lys-78 to 36% for Lys-11 in the A subunit and from 5% for Lys-82 to an av. of 38% for the peptide contg. Lys-166, Lys-174 and Lys-175 in the B subunit. Amino acid anal. demonstrated a single modification reaction producing N.epsilon.-(carboxymethyl)lysine. This agreed with the mass increase of 58 obsd. for each modified peptide.

L18 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1984:607688 HCAPLUS
DOCUMENT NUMBER: 101:207688
TITLE: Biosynthesis of esterified alkan-2-ols and .beta.-diketones in barley spike epicuticular wax: synthesis of radioactive intermediates
AUTHOR(S): Mikkelsen, Joern Dalgaard
CORPORATE SOURCE: Dep. Physiol., Carlsberg Lab., Copenhagen Valby, DK-2500, Den.
SOURCE: Carlsberg Res. Commun. (1984), 49(3), 391-416
CODEN: CRCODS; ISSN: 0105-1938
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirteen different 14C- and 3H-labeled epicuticular wax precursors were synthesized and their structures detd. by gas chromatog.-mass **spectrometry** analyses. The biosyntheses of .beta.-diketones and alkan-2-ol-contg. esters were studied by incorporating these intermediates into tissue slices of barley spikes whose awns had been removed. A **differential labeling** pattern of the alkan-2-ol esters and the .beta.-diketones was obsd. after feeding 3 selected mutants blocked in different steps catalyzed by a multifunctional enzyme encoded for by the cer-cqu gene. In cer-u69 tissue slices, (9,10-3H)-3-oxopalmitoyl-CoA was incorporated into both the esterified alkan-2-ols and the .beta.-diketones. Only the former wax component was synthesized by the mutants cer-c36 and -q42. When C14 and C16 fatty acyl chains were fed to the tissue slices, those of cer-u69 and -c36 readily labeled the esterified alkan-2-ols, whereas those of cer-q42 were totally inactive. In all 3 mutants, (2-14C)-pentadecan-2-one, (10,11-3H)-heptadecan-2-one,

and (2-3H)-pentadecan-2-ol exclusively labeled the alkan-2-ol moieties of the specified esters. (9,10-3H)-L-3-Hydroxypalmitoyl-CoA and (3-14C)-labeled DL-3-hydroxy fatty acids having 14, 16 and 18 C atoms were incorporated with a very low efficiency into the .beta.-diketones and the esterified alkan-2-ols. (9,10-3H)-3-oxopalmitoyl-CoA is the primer for the enzyme system known as .beta.-ketoacyl elongase which forms the C29 (nonacosan-14,16-dione), C31 (hentriacontan-14,16-dione), and C33 (tritriacontan-16,18-dione) .beta.-diketones. After protection of the .beta.-dicarbonyl group, 7 or 8 C2 units are added before the presumed decarboxylation to yield the complete .beta.-diketone carbon chain. The alkan-2-ol esters arise from the 3-oxoacyl-CoA deriv. by an initial decarboxylation to form a Me ketone, followed by a redn. to an alkan-2-ol. The latter is then esterified with a fatty acid to form the alkan-2-ol-contg. esters. The 3 steps involved in the alkan-2-ol ester synthesis are accomplished by the coordinated action of a decarboxylase, reductase, and ester synthetase.

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L15        10591 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (PROTEOME OR PROTEIN)(W)ANALYS
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L16         1278 SEA FILE=HCAPLUS ABB=ON  PLU=ON  PROTEIN(W)MASS(W)TAG OR PMT
L17          113 SEA FILE=HCAPLUS ABB=ON  PLU=ON  ISOTOPE(W)CODED(W)AFFINITY(W)T
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L18            8 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (DIFFERENTIAL(W)LABEL?)(L)SPEC
                 TROMET?
L25           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L17 AND (L14 OR L15 OR L16)
L26           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L25 NOT L18


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L26  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:326448  HCAPLUS
TITLE:                    Quantitative proteome analysis by
                          solid-phase isotope tagging and mass spectrometry
AUTHOR(S):                Zhou, H.; Ranish, J. A.; Watts, J. D.; Aebersold, R.
CORPORATE SOURCE:         Institute for Systems Biology, 1441 North 34th Street,
                          Seattle, WA, 98103-8904., USA
SOURCE:                   Nature Biotechnology (2002), 20(5), 512-515
                          CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER:                Nature America Inc.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   The adaptation of sequences of chem. reactions to a solid-phase format has
     been essential to the automation, reproducibility, and efficiency of a no.
     of biotechnol. processes including peptide and oligonucleotide synthesis
     and sequencing. Here we describe a method for the site-specific, stable
     isotopic labeling of cysteinyl peptides in complex peptide mixts. through
     a solid-phase capture and release process, and the concomitant isolation
     of the labeled peptides. The recovered peptides were analyzed by
     microcapillary liq. chromatog. and tandem mass spectrometry (.mu.LC-MS/MS)
     to det. their sequences and relative quantities. The method was used to
     detect galactose-induced changes in protein abundance in the yeast
     Saccharomyces cerevisiae. A side-by-side comparison with the
     isotope-coded affinity tag (
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ICAT) method demonstrated that the solid-phase method for stable isotope tagging of peptides is comparatively simpler, more efficient, and more sensitive.

L26 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:124090 HCAPLUS
TITLE: Mass spectrometry in coupling with affinity capture-release and **isotope-coded affinity tags** for quantitative **protein analysis**
AUTHOR(S): Turecek, Frantisek
CORPORATE SOURCE: Department of Chemistry, University of Washington, Seattle, WA, 98195-1700, USA
SOURCE: Journal of Mass Spectrometry (2002), 37(1), 1-14
CODEN: JMSPFJ; ISSN: 1076-5174
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Affinity capture-release electrospray ionization mass spectrometry (ACESIMS) and **isotope-coded affinity tags** (**ICAT**) are two recently introduced techniques for the quantitation of protein activity and content with applications to clin. enzymol. and functional proteomics, resp. One common feature of these methods is that they use biotinylated tags that function as mol. handles for highly selective and reversible affinity capture of conjugates from complex biol. mixts. such as cell homogenates and sub-cellular organelles. ACESIMS uses synthetic substrate conjugates specifically to target cellular enzymes that, when deficient, are the cause of genetic diseases. Multiplex detn. of enzyme activities is used for the diagnosis of lysosomal storage diseases. The **ICAT** method relies on selective conjugation of cysteine thiol groups in proteins, followed by enzymic digestion and quant. anal. of peptide conjugates by mass spectrometry. Another common feature of the ACESIMS and **ICAT** approaches is that both use conjugates labeled with stable heavy isotopes as internal stds. for quantitation. Selected applications of the ACESIMS and **ICAT** techniques are presented that include mol.-level diagnosis of genetic diseases in children and quant. detn. of protein expression in cells.
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:44449 HCAPLUS
DOCUMENT NUMBER: 136:147258
TITLE: **Proteome analysis** of low-abundance proteins using multidimensional chromatography and **isotope-coded affinity tags**
AUTHOR(S): Gygi, Steven P.; Rist, Beate; Griffin, Timothy J.; Eng, Jimmy; Aebersold, Ruedi
CORPORATE SOURCE: Department of Cell Biology, Harvard Medical School, Boston, MA, 02115, USA
SOURCE: Journal of Proteome Research (2002), 1(1), 47-54
CODEN: JPROBS; ISSN: 1535-3893
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effectiveness of proteome-wide **protein identification** and quant. expression profiling is dependent on the

ability of the anal. methodologies employed to routinely obtain information on low-abundance proteins, as these are frequently of great biol. importance. Two-dimensional gel electrophoresis, the traditional method for **proteome anal.**, has proven to be biased toward highly expressed proteins. Recently, two-dimensional chromatog. of the complex peptide mixts. generated by the digestion of unsepd. protein samples has been introduced for the identification of their components, and **isotope-coded affinity tags** (**ICAT**) have been introduced to allow for accurate quantification of the components of protein mixts. by mass spectrometry. Here, we demonstrate that the combination of isotope coded affinity protein tags and multidimensional chromatog./mass spectrometry of tryptic peptide mixts. is capable of detecting and quantifying proteins of low abundance in complex samples.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:896292 HCAPLUS
DOCUMENT NUMBER: 136:98677
TITLE: Toward a high-throughput approach to quantitative proteomic analysis: expression-dependent **protein identification** by mass spectrometry
AUTHOR(S): Griffin, Timothy J.; Han, David K. M.; Gygi, Steven P.; Rist, Beate; Lee, Hookeun; Aebersold, Ruedi; Parker, Kenneth C.
CORPORATE SOURCE: Department of Molecular Biotechnology, University of Washington, Seattle, WA, USA
SOURCE: Journal of the American Society for Mass Spectrometry (2001), 12(12), 1238-1246
CODEN: JAMSEF; ISSN: 1044-0305
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **isotope-coded affinity tag** (**ICAT**) technol. enables the concurrent identification and comparative quant. anal. of proteins present in biol. samples such as cell and tissue exts. and biol. fluids by mass spectrometry. The initial implementation of this technol. was based on microcapillary chromatog. coupled online with electrospray ionization tandem mass spectrometry. This implementation lacked the ability to select proteins for identification based on their relative abundance and therefore to focus on differentially expressed proteins. In order to improve the sample throughput of this technol., we have developed a two-step approach that is focused on those proteins for which the abundance changes between samples: First, a new software program for the automated quantification of **ICAT** reagent labeled peptides analyzed by microcapillary electrospray ionization time-of-flight mass spectrometry dets. those peptides that differ in their abundance and second, these peptides are identified by tandem mass spectrometry using an electrospray quadrupole time-of flight mass spectrometer and sequence database searching. Results from the application of this approach to the anal. of differentially expressed proteins secreted from nontumorigenic human prostate epithelial cells and metastatic cancerous human prostate epithelial cells are shown.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:759856 HCAPLUS
DOCUMENT NUMBER: 136:98535
TITLE: Nowhere to hide
AUTHOR(S): O'Driscoll, Cath
CORPORATE SOURCE: Royal Society of Chemistry, UK
SOURCE: Chemistry in Britain (2001), 37(9), 26-28
CODEN: CHMBAY; ISSN: 0009-3106
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review discusses the new approaches for probing proteomes which make it easier for drug researchers to pinpoint useful protein targets. The characteristics of MudPIT, which detected a large no. of proteins, the **Isotope-coded affinity tag** (**ICAT**) reagents, 2D-GE anal., and the coupling of **ICAT** reagents with a state-of-the art MALDI quadrupole time-of-flight mass spectrometer (MALDI QqTOF), are discussed. The **ICAT** reagents make **protein identification** faster and less labor-intensive, and allows quantification even for low abundance and difficult-to-isolate proteins. The 2D-GE anal. has identified 502 proteins for the virus Haemophilus influenzae. The MALDI QqTOF is the approach that massively reduced the researchers' workload by sifting out only the differentially expressed proteins of interest for subsequent quantification and identification.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:737615 HCAPLUS
DOCUMENT NUMBER: 136:306330
TITLE: The **isotope-coded affinity tag** reagent method for quantitative proteomics
AUTHOR(S): Aerbersold, Ruedi; Gygi, Steven P.; Griffin, Timothy J.; Han, David. K. M.; Yelle, Michael J.
CORPORATE SOURCE: Univ. of Washington, Seattle, WA, USA
SOURCE: American Genomic/Proteomic Technology (2001), 1(1), 22, 24, 26-27
CODEN: AGTMC7; ISSN: 1537-0003
PUBLISHER: International Scientific Communications, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **Isotope-coded Affinity Tag** (**ICAT**) reagent method, first described by Gygi et al. and recently commercialized by Applied Biosystems (Foster City, CA) enables the concurrent quantification and identification of proteins in complex mixts. It is based on a new class of chem. reagents termed **isotope-coded affinity tags** used in conjunction with tandem MS and multidimensional liq. chromatog. The method addresses several limitations of two-dimensional PAGE (2D-PAGE)-based proteomic expts. It has been shown to successfully identify and quantify both low-abundance and membrane proteins, classes that are typically difficult to analyze by 2D-PAGe. Automation is enabled by using a tandem MS instrument (API QSTARTM system with oMaldiTM and electrospray ion sources, from Applied Biosystems and MDS Sciex [Toronto, Ontario, Canada]) for performing expression-dependent **protein identification**

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:695694 HCAPLUS
DOCUMENT NUMBER: 135:300592
TITLE: Optimization of the **isotope-coded affinity tag**-labeling procedure for quantitative **proteome analysis**
AUTHOR(S): Smolka, Marcus B.; Zhou, Huilin; Purkayastha, Subhasish; Aebersold, Ruedi
CORPORATE SOURCE: Departamento de Bioquimica, Instituto de Biologia, Universidade Estadual de Campinas, Campinas, Sao Paulo, Brazil
SOURCE: Analytical Biochemistry (2001), 297(1), 25-31
CODEN: ANBCA2; ISSN: 0003-2697
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The combination of **isotope coded affinity tag** (**ICAT**) reagents and tandem mass spectrometry constitutes a new method for quant. proteomics. It involves the site-specific, covalent labeling of proteins with isotopically normal or heavy **ICAT** reagents, proteolysis of the combined, labeled protein mixt., followed by the isolation and mass spectrometric anal. of the labeled peptides. The method critically depends on labeling protocols that are specific, quant., general, robust, and reproducible. Here we describe the systematic evaluation of important parameters of the labeling protocol and describe optimized labeling conditions. The tested factors include the **ICAT** reagent concn., the influence of the protein, SDS, and urea concns. on the labeling reaction, and the reaction time. We demonstrate that using the optimized conditions specific and quant. labeling was achieved on std. proteins as well as in complex protein mixts. such as a yeast cell lysate. (c) 2001 Academic Press.
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:197242 HCAPLUS
TITLE: Novel tools for the field of proteomics
AUTHOR(S): Martin, Stephen A.; Vestal, Marvin; Juhasz, Peter; Williamson, Brian; Marchese, Jason; Graber, Armin; Patterson, Dale
CORPORATE SOURCE: Proteomics Research Center, Applied Biosystems, Framingham, MA, 01701, USA
SOURCE: Abstr. Pap. - Am. Chem. Soc. (2001), 221st, ANYL-155
CODEN: ACSRAL; ISSN: 0065-7727
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English
AB Proteomics encompasses a broad range of technologies aimed at detg. the identity and quantity of expressed protein in cells, their three-dimensional structure and interaction partners. Intense focus has been placed on the development of a series of processes that will enable researchers to complete these studies with appropriate sensitivity and throughput to leverage the corresponding genomics information. In the subset of proteomics focused on **protein identification** and quantification we have been investigating a series of novel technologies that may accelerate the overall work flow in Proteomics. Two key areas include **isotope coded affinity tags** (**ICAT**) and matrix assisted laser desorption ionization tandem time of flight (MALDI TOF/TOF). The **ICAT**

reagent enables rapid relative quantification of protein expression without the requirement for 2D-gel electrophoresis. MADLI TOF/TOF couples a high throughput mode of ionization with tandem mass spectrometry. This combination provides both mol. mass and primary sequence information with MALDI.

L26 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:172543 HCAPLUS
DOCUMENT NUMBER: 134:350140
TITLE: Matrix-assisted laser desorption/ionization coupled with quadrupole/orthogonal acceleration time-of-flight mass spectrometry for protein discovery, identification, and structural analysis
AUTHOR(S): Baldwin, Michael A.; Medzihradszky, Katalin F.; Lock, Chris M.; Fisher, Bill; Settineri, Tina A.; Burlingame, A. L.
CORPORATE SOURCE: Mass Spectrometry Facility Department of Pharmaceutical Chemistry, University of California, San Francisco, CA, 94143-0446, USA
SOURCE: Analytical Chemistry (2001), 73(8), 1707-1720
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The design and operation of a novel UV-MALDI ionization source on a com. QqoaTOF mass spectrometer (Applied Biosystem/MDS Sciex QSTAR Pulsar) is described. Samples are loaded on a 96-well target plate, the movement of which is under software control and can be readily automated. Unlike conventional high-energy MALDI-TOF, the ions are produced with low energies (5-10 eV) in a region of relatively low vacuum (8 mTorr). Thus, they are cooled by extensive low-energy collisions before selection in the quadrupole mass analyzer (Q1), potentially giving a quasi-continuous ion beam ideally suited to the oaTOF used for mass anal. of the fragment ions, although ion yields from individual laser shots may vary widely. Ion dissocn. is induced by collisions with argon in an rf-only quadrupole cell, giving typical low-energy CID spectra for protonated peptide ions. Ions sepd. in the oaTOF are registered by a four-anode detector and time-to-digital converter and accumulated in "bins" that are 625 ps wide. Peak shapes depend upon the no. of ion counts in adjacent bins. As expected, the accuracy of mass measurement is shown to be dependent upon the no. of ions recorded for a particular peak. With internal calibration, mass accuracy better than 10 ppm is attainable for peaks that contain sufficient ions to give well-defined Gaussian profiles. By virtue of its high resoln., capability for accurate mass measurements, and sensitivity in the low-femtomole range, this instrument is ideally suited to **protein identification** for proteomic applications by generation of peptide tags, manual sequence interpretation, identification of modifications such as phosphorylation, and protein structural elucidation. Unlike the multiply charged ions typical of electrospray ionization, the singly charged MALDI-generated peptide ions show a linear dependence of optimal collision energy upon mol. mass, which is advantageous for automated operation. It is shown that the novel pulsing technique of this instrument that increases the sensitivity for precursor ions scans is applicable to the identification of peptides labeled with **isotope-coded affinity tags**.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:79420 HCAPLUS
DOCUMENT NUMBER: 134:219186
TITLE: Quantitative proteomic analysis using a MALDI quadrupole time-of-flight mass spectrometer
AUTHOR(S): Griffin, Timothy J.; Gygi, Steven P.; Rist, Beate; Aebersold, Ruedi; Loboda, Alexander; Jilkine, Alexandra; Ens, Werner; Standing, Kenneth G.
CORPORATE SOURCE: Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195-7730, USA
SOURCE: Analytical Chemistry (2001), 73(5), 978-986
CODEN: ANCHAM; ISSN: 0003-2700
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We describe an approach to the quant. anal. of complex protein mixts. using a MALDI quadrupole time-of-flight (MALDI QqTOF) mass spectrometer and **isotope coded affinity tag** reagents (Gygi, S. P.; et al. Nat. Biotechnol. 1999, 17, 994-9.). Proteins in mixts. are first labeled on cysteinyl residues using an **isotope coded affinity tag** reagent, the proteins are enzymically digested, and the labeled peptides are purified using a multidimensional sepn. procedure, with the last step being the elution of the labeled peptides from a microcapillary reversed-phase liq. chromatog. column directly onto a MALDI sample target. After addn. of matrix, the sample spots are analyzed using a MALDI QqTOF mass spectrometer, by first obtaining a mass spectrum of the peptides in each sample spot in order to quantify the ratio of abundance of pairs of isotopically tagged peptides, followed by tandem mass spectrometric anal. to ascertain the sequence of selected peptides for **protein identification**. The effectiveness of this approach is demonstrated in the quantification and identification of peptides from a control mixt. of proteins of known relative concns. and also in the comparative anal. of protein expression in Saccharomyces cerevisiae grown on two different carbon sources.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:894688 HCAPLUS
DOCUMENT NUMBER: 134:292351
TITLE: The **proteome**: **analysis** and utility
AUTHOR(S): Aebersold, Ruedi; Rist, Beate; Gygi, Steven P.
CORPORATE SOURCE: Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 393-395. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB With the completion of a rapidly increasing no. of genomic sequences much attention is currently focused on the questions if and how the information contained in sequence databases can be interpreted in terms of the structure, function and control of biol. systems. Quant. **proteome anal.**, the global anal. of protein expression, has been proposed

as a method to study steady state and perturbation-induced changes in gene expression. It is shown that in the emerging post-genomic era, technologies that can quant., globally, and automatically measure gene expression at the protein level are essential for the comprehensive anal. of biol. processes and systems. Furthermore, the limitations of the current std. method for large-scale **protein anal.** with respect to the anal. of low abundance proteins are documented, and a new approach to quant. **proteome anal.** is proposed.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:548383 HCAPLUS
DOCUMENT NUMBER: 133:249085
TITLE: Proteome profiling-pitfalls and progress
AUTHOR(S): Haynes, Paul A.; Yates, John R., III
CORPORATE SOURCE: Novartis Agricultural Discovery Institute, San Diego, CA, 92121, USA
SOURCE: Yeast (2000), 17(2), 81-87
CODEN: YESTE3; ISSN: 0749-503X
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 51 refs. In this review we examine the current state of anal. methods in proteomics. The conventional methodol. using two-dimensional electrophoresis gels and mass spectrometry is discussed, with particular ref. to the advantages and shortcomings thereof. Two recently published methods which offer an alternative approach are presented and discussed, with emphasis on how they can provide information not available via two-dimensional gel electrophoresis. These two methods are the **isotope-coded affinity tags** approach of Gygi et al. and the two-dimensional liq. chromatog.-tandem mass spectrometry approach as presented by Link et al. We conclude that both of these new techniques represent significant advances in anal. methodol. for **proteome anal.** Furthermore, we believe that in the future biol. research will continue to be enhanced by the continuation of such developments in proteomic anal. technol.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:390113 HCAPLUS
DOCUMENT NUMBER: 134:142438
TITLE: New approaches to quantitative **proteome analysis**
AUTHOR(S): Aebersold, Ruedi; Rist, Beate; Gygi, Steven P.
CORPORATE SOURCE: Department of Molecular Biotechnology, University of Washington, Seattle, WA, 98195, USA
SOURCE: Biotecnologia Aplicada (2000), 17(1), 46-47
CODEN: BTAPEP; ISSN: 0864-4551
PUBLISHER: Elfos Scientiae
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Levels of protein expression encoded by mRNA with comparable abundance varied by as much as 30-fold in exponentially growing Saccharomyces cerevisiae. In this same system, levels of mRNA coding for protein with comparable expression levels varied by as much as 20-fold. This indicates that mRNA anal. alone is insufficient to describe protein expression. Comparison of codon bias distributions for all yeast ORFs with

distribution of all proteins analyzed by std. 2-dimensional gel electrophoresis (2DE), silver staining, and tandem mass spectrometry (MS/MS) found a large bias towards the most highly expressed proteins when using 2DE/MS/MS. The use of **isotope-coded affinity tags** (**ICAT**) and MS/MS addresses the limitation inherent in 2DE/MS/MS.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L26 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:683625 HCAPLUS
DOCUMENT NUMBER: 132:47167
TITLE: Quantitative analysis of complex protein mixtures using **isotope-coded affinity tags**
AUTHOR(S): Gygi, Steven P.; Rist, Beate; Gerber, Scott A.; Turecek, Frantisek; Gelb, Michael H.; Aebersold, Ruedi
CORPORATE SOURCE: Dep. Mol. Biotechnol., Univ. Washington, Seattle, WA, 98195-7730, USA
SOURCE: Nature Biotechnology (1999), 17(10), 994-999
CODEN: NABIF9; ISSN: 1087-0156
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We describe an approach for the accurate quantification and concurrent sequence identification of the individual proteins within complex mixts. The method is based on a class of new chem. reagents termed **isotope-coded affinity tags** (**ICATs**) and tandem mass spectrometry. Using this strategy, we compared protein expression in the yeast Saccharomyces cerevisiae, using either ethanol or galactose as a carbon source. The measured differences in protein expression correlated with known yeast metabolic function under glucose-repressed conditions. The method is redundant if multiple cysteinyl residues are present, and the relative quantification is highly accurate because it is based on stable isotope diln. techniques. The **ICAT** approach should provide a widely applicable means to compare quant. global protein expression in cells and tissues.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT